Banff International Research Station
for Mathematical Innovation and Discovery

# Soft Matter Simulation of Cell Motility


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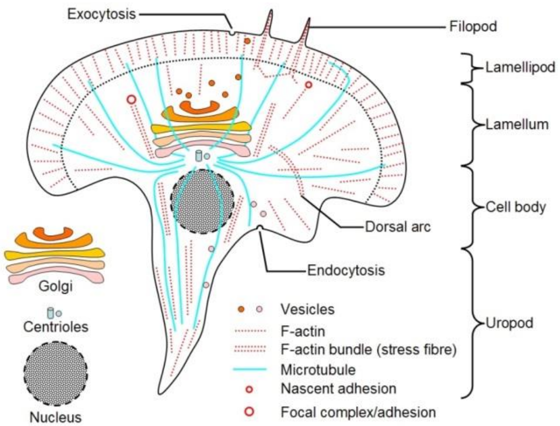
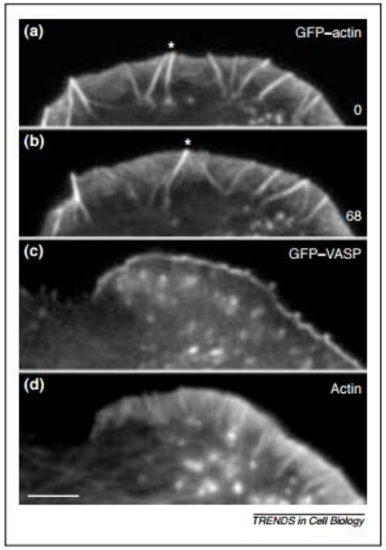
# I. Introduction

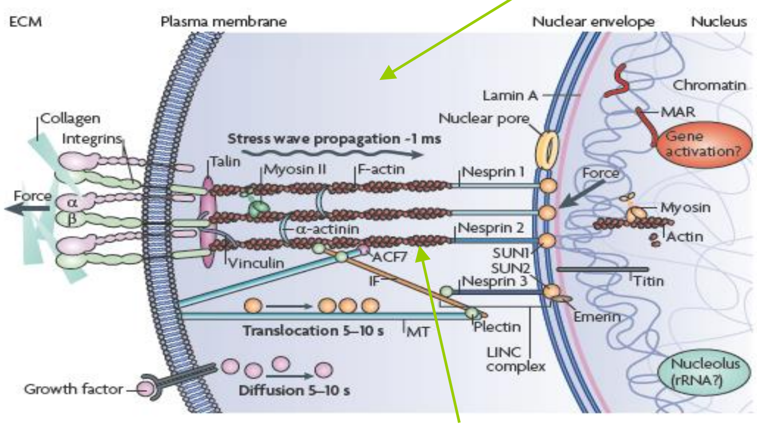



Small et. al. (2002)

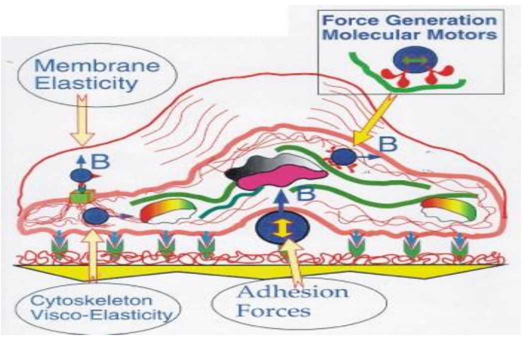
Retrograde flow in lamellipodia motion

Liquid like medium



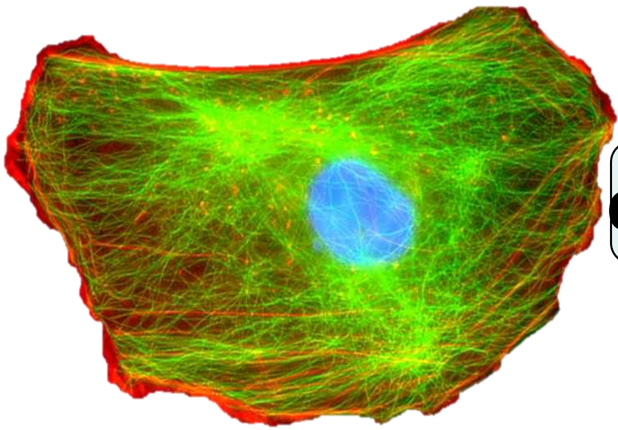

Cytoskeleton

*Ning Wang et al. Natural Reviews Molecular Cell Biology [2009]*

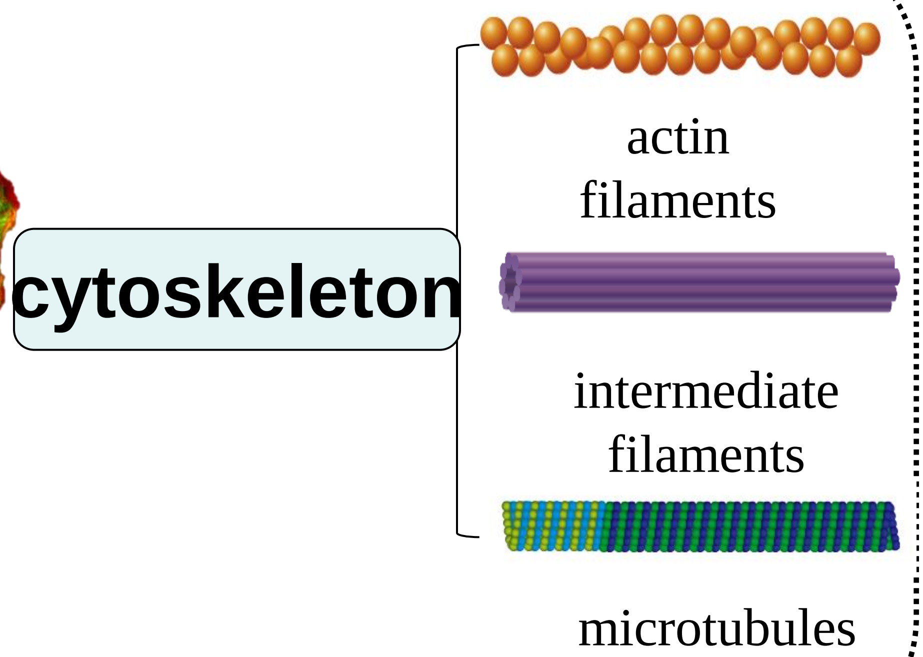



***Ligand-receptor interactions***

# II. How to model Cytoskeleton ?

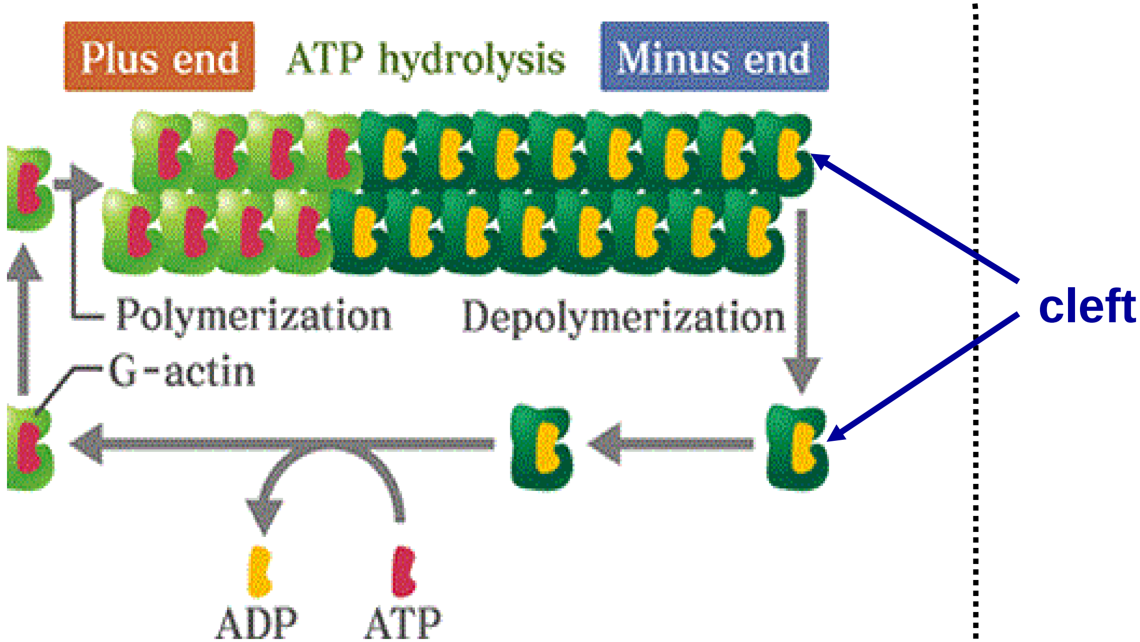


**Cell cytoskeleton**



# How to model actin filament:
# (ATP) Hydrolysis of Actin filaments

**Actin-filament is polarized because the cleft is always towards the minus end.**




**Dynamics of the actin-filaments**

# Hydrodynamics of active polar gel

The strong forms of an active nematic gel hydrodynamics are

$$
\begin{aligned}
\rho_f \frac{D\mathbf{v}}{Dt} &= \nabla \cdot \boldsymbol{\sigma} + \mathbf{b}, \quad \forall\, \mathbf{x} \in V(t) \\
\rho_d \frac{D\tilde{\mathbf{h}}}{Dt} &= \lambda \mathbf{d} \cdot \mathbf{h} - \mathbf{w} \cdot \mathbf{h} + \gamma \nabla \cdot \boldsymbol{\nabla} \otimes \mathbf{h}, \ \ \forall\, \mathbf{x} \in V(t)
\end{aligned}
$$

where the Cauchy stress is given as

**liquid**

$$
\begin{aligned}
\boldsymbol{\sigma} &= \boldsymbol{\sigma}^p + \boldsymbol{\sigma}^a \\
\boldsymbol{\sigma}^p &= -p\mathbf{I} + 2\mu\mathbf{d} - \frac{\lambda}{2}\Big(\mathbf{h} \otimes \mathbf{s} + \mathbf{s} \otimes \mathbf{h}\Big) + \frac{1}{2}\Big(\mathbf{h} \otimes \mathbf{s} + \mathbf{s} \otimes \mathbf{h}\Big) \\
\boldsymbol{\sigma}^a &= -\zeta \mathbf{h} \otimes \mathbf{h}
\end{aligned}
$$

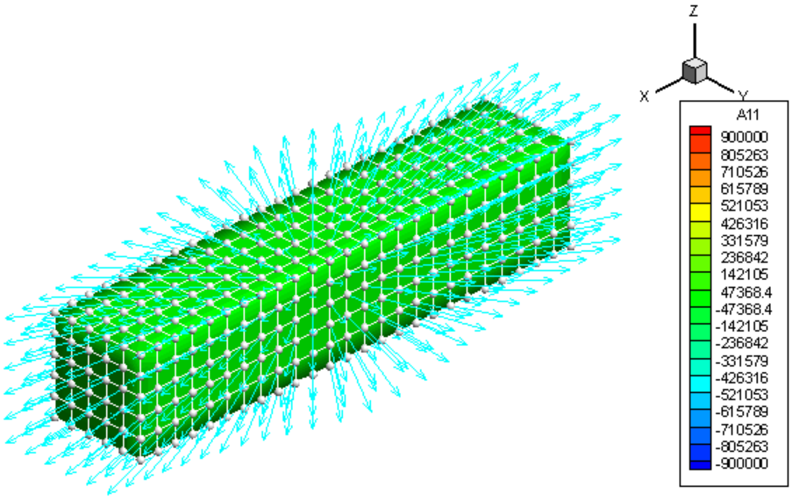
where $\mathbf{s} = K\nabla^2\mathbf{h}$ and the term

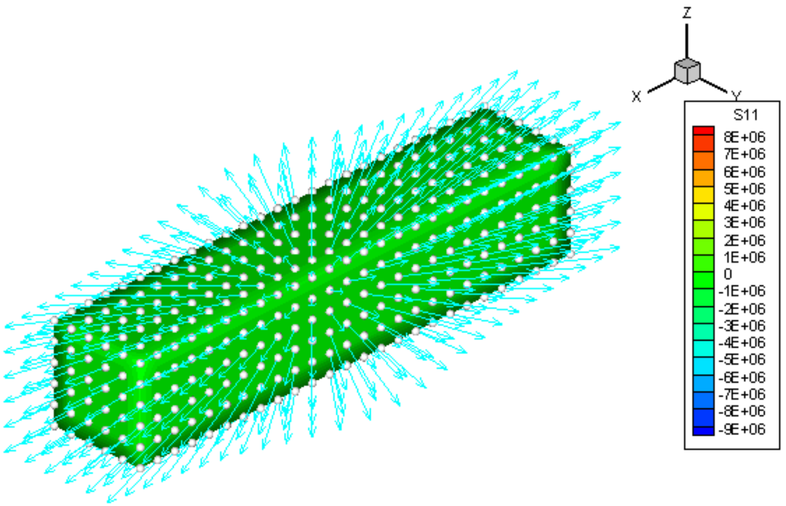
**polarity**

$\boldsymbol{\sigma}^{active} = -\zeta \mathbf{h} \otimes \mathbf{h}$ **is the active stress.**

Reference: Voituriez, Jonnay, and Prost [2005];
Jülicher, Kruse, Prost, and Joanny [2007].

# Active stress



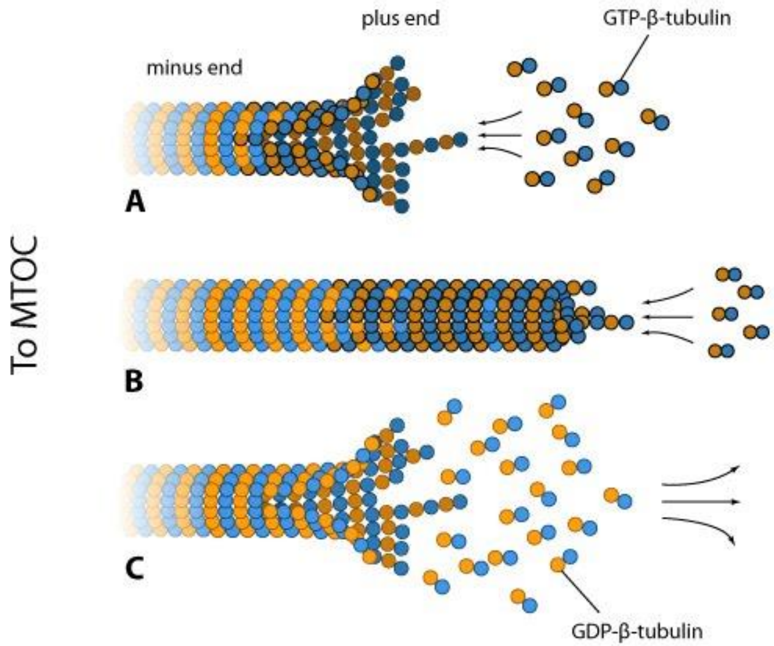




**(a) Active Stress**

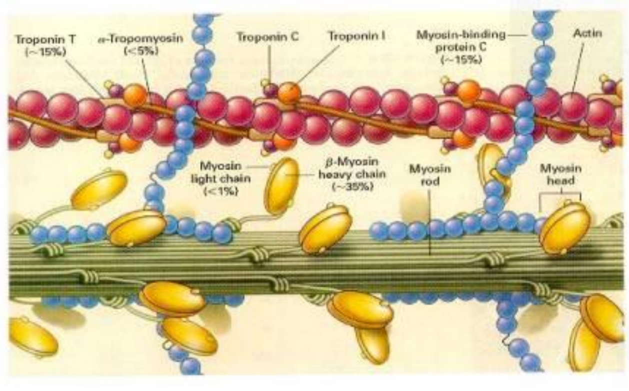
**(b) Total stress response**

# Modeling Microtubles and actin filaments

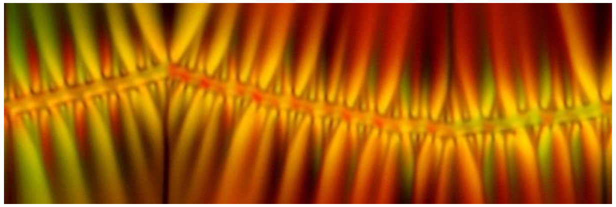
## GTP Hydrolysis

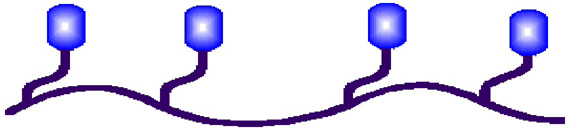



**We are modeling microtubules as liquid crystal elastomer.**



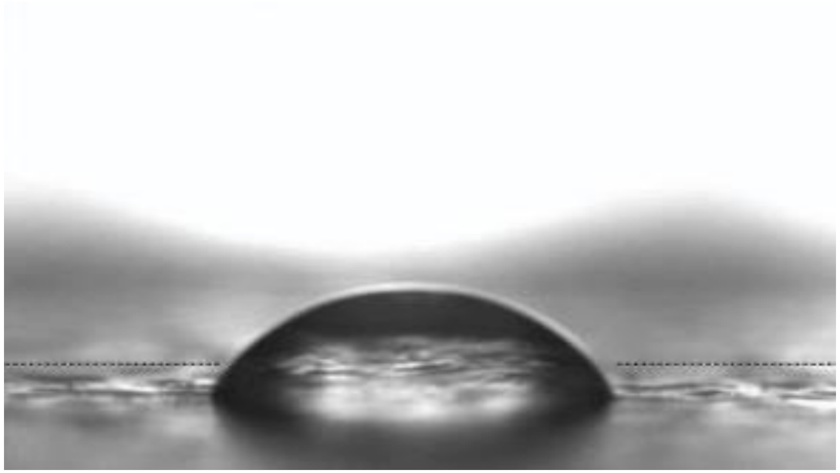

Actomyosin molecules in a cell



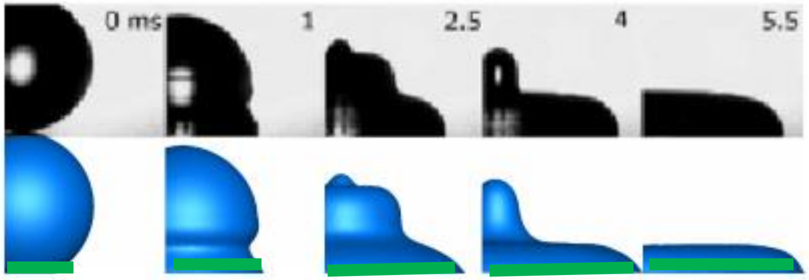


Mesogen in nematic LCE

# III. Multiscale Moving Contact Line Theory



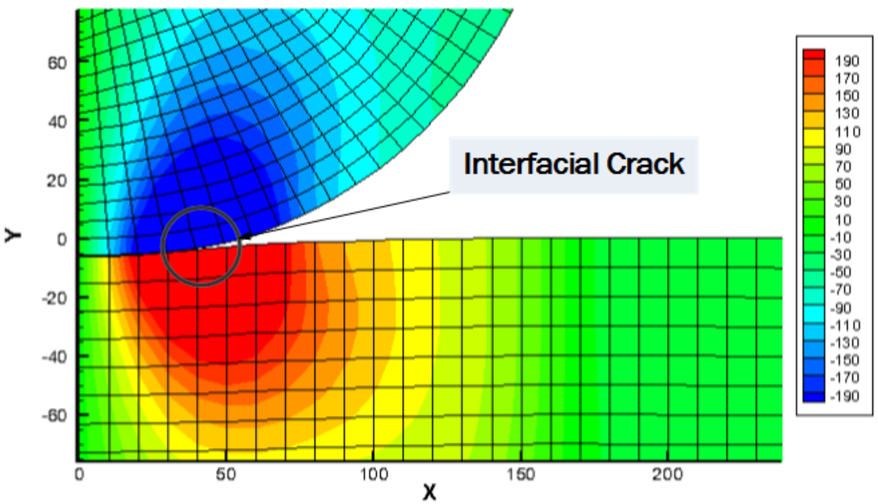
Diffused Interface Phase-field Modeling

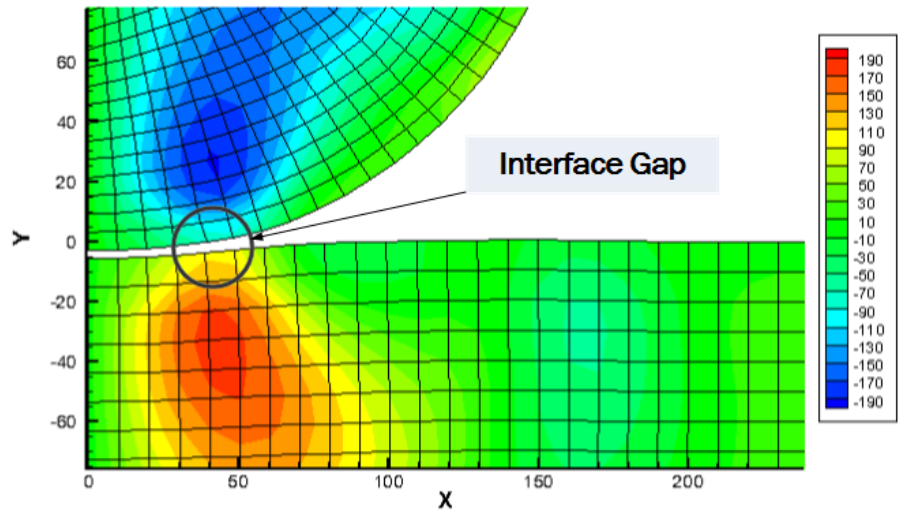



(b) $\theta_e$=50°

Margrit Klitz (2014)

# Basic Idea

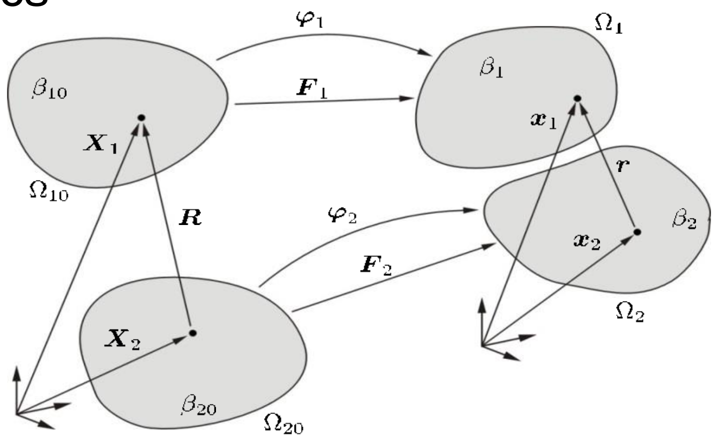



**Conventional mving contact-line theory and Multiscale moving contact-line theory**

# Multiscale contact/adhesion model

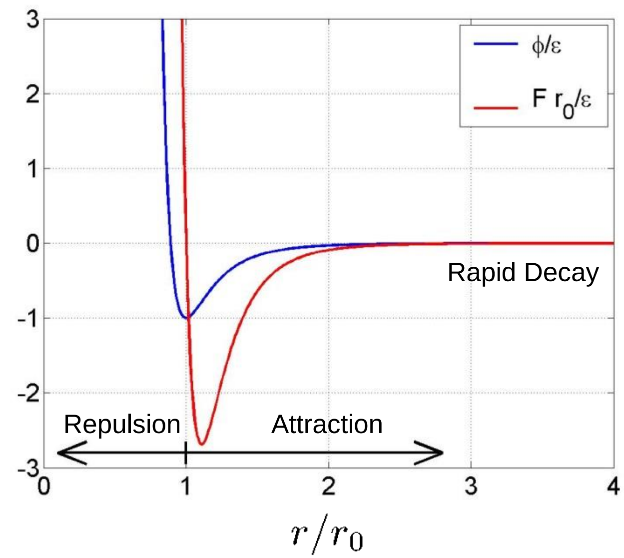
Kinematics




Lennard-Jones Potential

$$\phi(r) = \epsilon\left(\frac{r_0}{r}\right)^{12} - 2\epsilon\left(\frac{r_0}{r}\right)^{6}$$

$$F(r) = -\frac{\partial \phi}{\partial r}$$




$\phi(r)$ - yields the Interaction Energy of $\Omega_1$ and $\Omega_2$

$$\Pi_{\mathrm{C}} = -\int_{\Omega_1}\int_{\Omega_2} \beta_1\ \beta_2\ \phi(\boldsymbol{x}_1 - \boldsymbol{x}_2)\ dv\ dv$$

$\psi(r)$ - yields the Internal Energy of the two bodies

$$\Pi_{\mathrm{int},1} = \int_{\Omega_1} W_1(\psi_1)\ dv$$

$$W_1 := \frac{\beta_1}{2}\sum_{j\neq i}^{n_1} \psi_1(x_1 - \mathbf{z}_j)$$

# Variational Principle

Interaction Potential

$$\Pi_{\mathrm{C}} = -\int_{\Omega_1}\int_{\Omega_2} \beta_1\beta_2\;\phi(r)\;dv\;dv$$

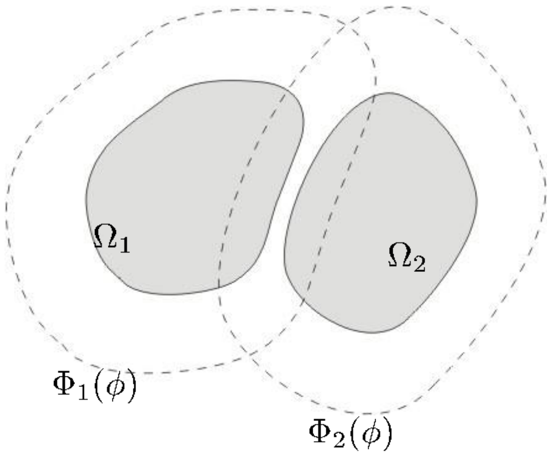
Principle of virtual Work

$$\Pi = \sum_{I=1}^{2}\left[\Pi_{\mathrm{int},I} - \Pi_{\mathrm{ext},I}\right] - \Pi_{\mathrm{C}}$$

$$\delta\Pi = 0\;, \quad \forall\;\delta\boldsymbol{\varphi}_I$$

Variation

$$\begin{aligned}\delta\Pi_{\mathrm{C}} &= -\int_{\Omega_1}\int_{\Omega_2} \beta_1\beta_2\Big(\frac{\partial\phi(r)}{\partial\boldsymbol{x}_1}\cdot\delta\boldsymbol{\varphi}_1 + \frac{\partial\phi(r)}{\partial\boldsymbol{x}_2}\cdot\delta\boldsymbol{\varphi}_2\Big)\;dv\;dv \\ &= \int_{\Omega_1}\delta\boldsymbol{\varphi}_1\cdot\beta_1\boldsymbol{b}_1\;dv + \int_{\Omega_2}\delta\boldsymbol{\varphi}_2\cdot\beta_2\boldsymbol{b}_2\;dv\end{aligned}$$




Adhesive Body Forces

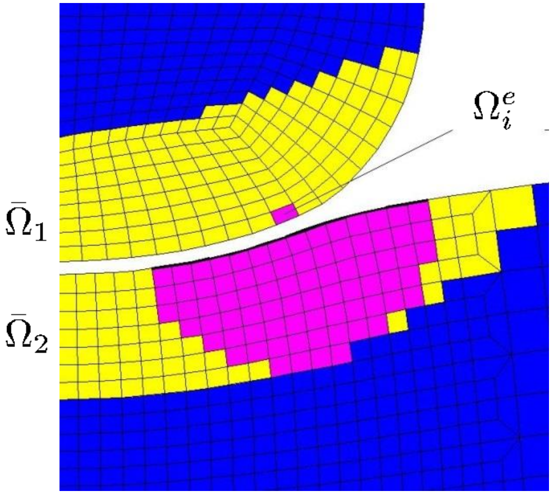
$$\boldsymbol{b}_1(\boldsymbol{x}_1) := -\frac{\partial\Phi_2}{\partial\boldsymbol{x}_1}\;, \qquad \Phi_2 := \int_{\Omega_2}\beta_2\;\phi(r)\;dv$$

$$\boldsymbol{b}_2(\boldsymbol{x}_2) := -\frac{\partial\Phi_1}{\partial\boldsymbol{x}_2}\;, \qquad \Phi_1 := \int_{\Omega_1}\beta_1\;\phi(r)\;dv$$

# Convert body-to-body interaction into Surface-to-surface interaction: Derjaquin Approximation

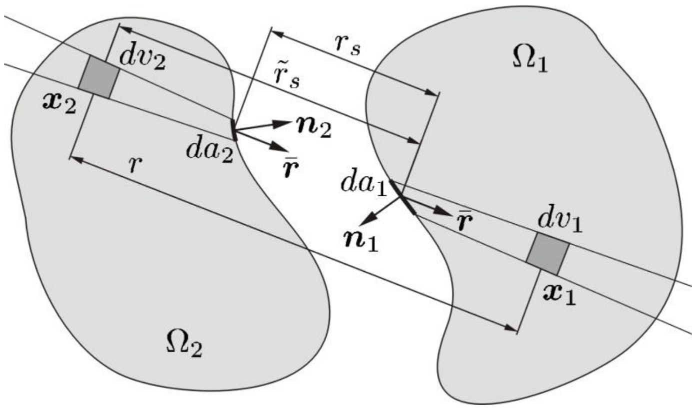
$$\mathbf{f}_{C,i} = \int_{\Omega_i^e} \int_{\Omega_j^e} \mathbf{N}_i^T \beta_i \beta_j \frac{\partial \phi}{\partial \boldsymbol{x}_i} \, dv \, dv$$

## Method 1




→ the number of interacting elements can become large

## Method 2 : Project volume integration onto surface




$$dv_1 dv_2 = -\frac{r}{r_s} dr \, d\tilde{r} \, (\bar{\boldsymbol{r}} \cdot \boldsymbol{n}_1)(\bar{\boldsymbol{r}} \cdot \boldsymbol{n}_2) \, da_1 da_2$$

→ Integrate $r$-Direction analytically

## Interaction Force Vector

$$\mathbf{f}_{C,i} = -\int_{\Gamma_i^e} \int_{\Gamma_j^e} \mathbf{N}_i^T \, \beta_i \beta_j \, \psi_s(r_s) \bar{\boldsymbol{r}} \, (\bar{\boldsymbol{r}} \cdot \boldsymbol{n}_1)(\bar{\boldsymbol{r}} \cdot \boldsymbol{n}_2) \, da \, da$$

$$\psi_s(r_s) := -\lim_{r_c \to \infty} \frac{1}{r_s} \int_{r_s}^{r_c} \int_{\tilde{r}_s}^{r_c} r \, \frac{\partial \phi(r)}{\partial r} \, dr \, d\tilde{r}_s$$

**For LJ potential**

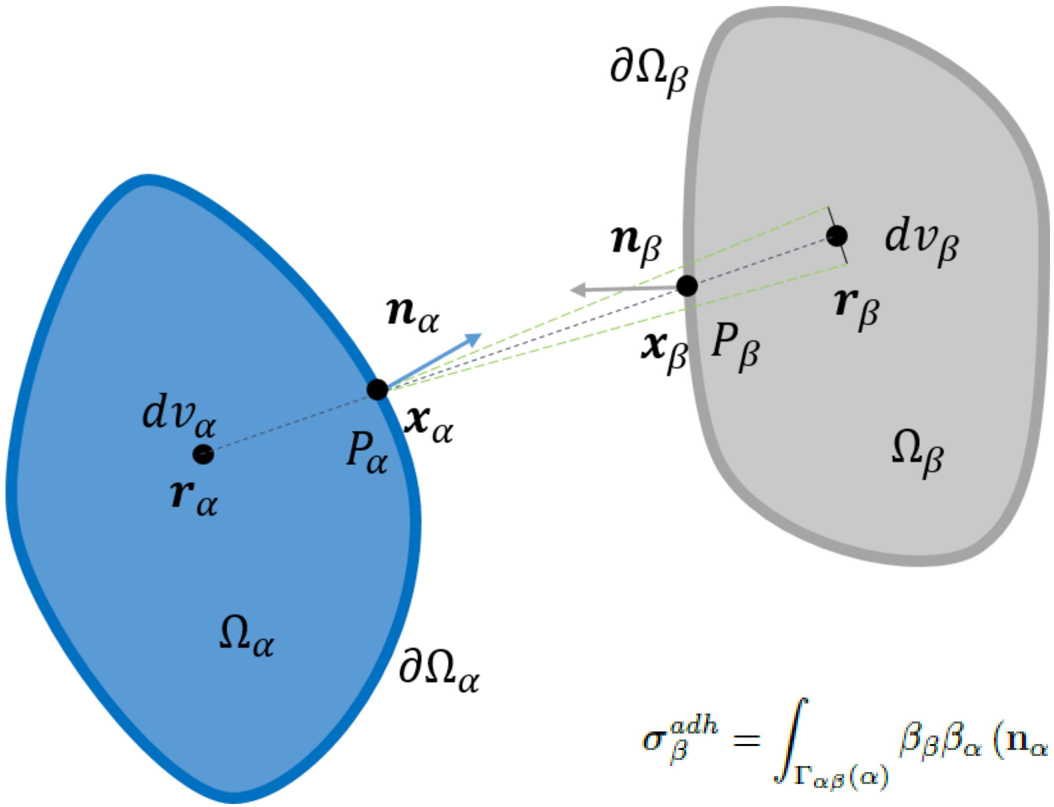
$$\psi(s) = \frac{2}{3} \varepsilon \left[ \frac{1}{6} \left( \frac{\sigma_0}{s} \right)^{12} - \left( \frac{\sigma_0}{s} \right)^6 \right]$$

# Surface Stress Tensor

$$d\mathbf{F}_\beta = \{\beta_\beta\beta_\alpha(\mathbf{n}_\alpha \otimes \mathbf{s}_{\beta\alpha}) \cdot \mathbf{n}_\beta \psi(s)\}\, da_\beta da_\alpha$$

$$\mathbf{s}_{\alpha\beta} = \mathbf{x}_\beta - \mathbf{x}_\alpha$$

$$\frac{d\mathbf{F}_\alpha}{da_\alpha} = \{\beta_\alpha\beta_\beta(\mathbf{n}_\beta \otimes \mathbf{s}_{\alpha\beta})\,\psi(s)da_\beta\} \cdot \mathbf{n}_\alpha$$



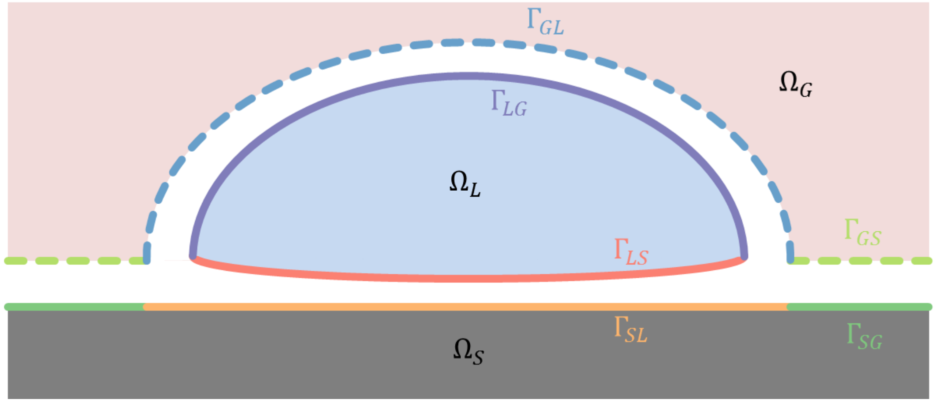

$$\boldsymbol{\sigma}_\alpha^{adh} = \int_{\Gamma_{\alpha\beta}(\beta)} \beta_\alpha\beta_\beta(\mathbf{n}_\beta \otimes \mathbf{s}_{\alpha\beta})\,\psi(s)da_\beta$$

$$\mathbf{t}_\alpha^{adh} = \boldsymbol{\sigma}_\alpha^{adh} \cdot \mathbf{n}_\alpha$$

$$\boldsymbol{\sigma}_\beta^{adh} = \int_{\Gamma_{\alpha\beta}(\alpha)} \beta_\beta\beta_\alpha(\mathbf{n}_\alpha \otimes \mathbf{s}_{\beta\alpha})\,\psi(s)da_\alpha, \quad \mathbf{t}_\beta^{adh} = \boldsymbol{\sigma}_\beta^{adh} \cdot \mathbf{n}_\beta,$$

**Fan and Li [2015] JCP**

# An Elasto-hydrodynamics Interface Theory



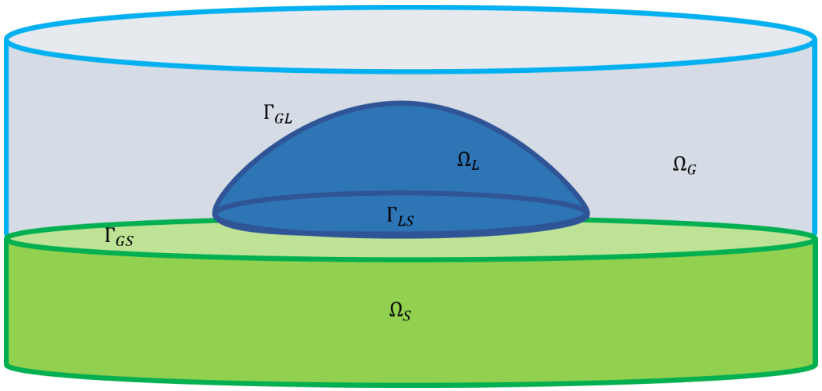

$$\mathbf{f}^{D,\alpha} := \nabla_s \varsigma_\alpha + \mathbf{t}^\alpha = \rho_{s\alpha} v_\alpha \mathbf{v}_\alpha, \quad \alpha = G, L, S$$

**Surface stress**

## An Extension of the Gurtin-Murdoch Surface Elasticity Theory

**Morton E. Gurtin**

**A. Ian Murdoch**




$$\nabla \cdot \boldsymbol{\sigma}_\alpha + \rho_\alpha \mathbf{b}_\alpha = \rho_\alpha \ddot{\mathbf{u}}_\alpha, \ \alpha = G, L, \ \text{and } S$$

For L-phase

$$\boldsymbol{\sigma} = \kappa_L (\ln J)\mathbf{I} + \mu_L \left( \nabla \otimes \mathbf{v} + (\nabla \otimes \mathbf{v})^T \right)$$

For S-phase

$$\mathbf{S} = \lambda_S \mathrm{Tr}(\mathbf{E})\mathbf{I} + 2\mu_S \mathbf{E},$$

Without considering interface diffusion and friction, we choose the following interface constitutive relations,

$$\varsigma_{LS} = \gamma_{LS}\mathbf{I}_s^{(2)} + \nabla_s \gamma_{LS}\mathbf{I}_s^{(2)} + \frac{\partial W_S}{\partial \epsilon_s} + \mu_{LS}\mathbf{d}_s + \gamma_{LS}\nabla_s \otimes \mathbf{u}; \tag{2.13}$$

$$\varsigma_{GL} = \gamma_{GL}\mathbf{I}_s^{(2)} + \nabla_s \gamma_{GL}\mathbf{I}_s^{(2)} + \mu_{GL}\mathbf{d}_s + \gamma_{GL}\nabla_s \otimes \mathbf{u}; \tag{2.14}$$

$$\varsigma_{GS} = \gamma_{LS}\mathbf{I}_s^{(2)} + \nabla_s \gamma_{GS}\mathbf{I}_s^{(2)} + \frac{\partial W_S}{\partial \epsilon_s} + \mu_{GS}\mathbf{d}_s + \gamma_{GS}\nabla_s \otimes \mathbf{u}; \tag{2.15}$$

where $\mathbf{u}$ are three-dimensional the surface displacements; $\gamma_{LS}, \gamma_{GL}$ and $\gamma_{GS}$ are the surface tension in different interfaces; the operator $\otimes$ is the standard notation for tensor

## This equation can be derived from diffused interface theory

$$\nabla_s \varsigma_{\alpha\beta} + [\mathbf{t}_\alpha] = \bar{\rho}_{\alpha\beta}(\mathbf{v}_\beta - \mathbf{v}_\alpha) v_\alpha^{intf}, \quad \forall \mathbf{x} \in \Gamma_{\alpha\beta}, \quad \alpha, \beta = G, L, S$$

$$\nabla_s := \nabla - \mathbf{n}_\alpha(\mathbf{n}_\alpha \cdot \nabla)$$

$$[\mathbf{t}_\alpha] = (\sigma_\alpha - \sigma_\beta)\mathbf{n}_\alpha \approx (\sigma_\alpha^{adh} - \sigma_\beta^{adh})\mathbf{n}_\alpha = [\mathbf{t}^{adh}]$$

For finite deformation:

$$W_s = \frac{1}{2}\epsilon_s : \mathbf{C}_s : \epsilon_s, \quad \mathbf{C}_s = C^s_{ijk\ell}\mathbf{e}_i \otimes \mathbf{e}_j \otimes \mathbf{e}_k \otimes \mathbf{e}_\ell, \quad \text{where}$$

$$C^s_{ijk\ell} = (\lambda_s + \gamma_s)\delta_{ij}\delta_{k\ell} + \mu_s(\delta_{ik}\delta_{j\ell} + \delta_{i\ell}\delta_{jk}), \quad i, j, k, \ell = 1, 2;$$

Subsequently, one can readily derive the interface constitutive relation in terms of surface displacements and velocities, for instance,

$$\begin{aligned} \varsigma_{LS} &= \gamma_{LS}\mathbf{I}_s^{(2)} + \nabla_s \gamma_{LS}\mathbf{I}_s^{(2)} + (\mu_S - \gamma_S)\mathbf{P}\Big(\nabla \otimes \mathbf{u} + (\nabla \otimes \mathbf{u})^T - (\nabla \otimes \mathbf{u})^T \nabla \otimes \mathbf{u}\Big)\mathbf{P} \\ &+ (\lambda_S + \gamma_S)\,\mathrm{Tr}\Big[\mathbf{P}\Big(\nabla \otimes \mathbf{u} + (\nabla \otimes \mathbf{u})^T - (\nabla \otimes \mathbf{u})^T \nabla \otimes \mathbf{u}\Big)\mathbf{P}\Big]\mathbf{I}_s^{(2)} \\ &+ \gamma_{LS}\nabla_a \otimes \mathbf{u} + \mu_{LS}\mathbf{P}\mathrm{Sym}\Big(\nabla \otimes \mathbf{v}\Big)\mathbf{P}\,. \end{aligned} \tag{2.19}$$

$$\epsilon = \frac{1}{2}(\mathbf{I} - \mathbf{b}^{-1}) \quad \text{and} \quad \mathbf{b} =: \mathbf{F} \cdot \mathbf{F}^T \qquad \epsilon_s := \mathbf{P} \cdot \epsilon \cdot \mathbf{P}$$

## 1. Monolithic solution

$$\nabla \cdot \boldsymbol{\sigma}_\alpha + \rho_\alpha \mathbf{b}_\alpha = \rho_\alpha \ddot{\mathbf{u}}_\alpha, \text{ and } \mathbf{t}_\alpha = \boldsymbol{\sigma}_\alpha \mathbf{n}_\alpha, \forall \mathbf{x} \in \partial\Omega_{\alpha t}$$
$$\nabla_s \cdot \varsigma_{\alpha\beta} + (\mathbf{t}_\alpha - \mathbf{t}_\beta) = \bar{\rho} v_\alpha^{inft} (\mathbf{v}_\beta - \mathbf{v}_\alpha); \ \forall \mathbf{x} \in \Gamma_{\alpha\beta} .$$
$$\nabla \cdot \boldsymbol{\sigma}_\beta + \rho_\beta \mathbf{b}_\beta = \rho_\beta \ddot{\mathbf{u}}_\beta, \text{ and } \mathbf{t}_\beta = \boldsymbol{\sigma}_\beta \mathbf{n}_\beta, \forall \mathbf{x} \in \partial\Omega_{\beta t}$$

## 2. Iterative solution

$$\mathbf{t}_\alpha = \bar{\rho} v_\alpha^{inf} (\mathbf{v}_\alpha - \mathbf{v}_\beta) - \nabla_s \cdot \varsigma_{\alpha\beta} - \mathbf{t}_\beta$$

$\beta \rightarrow \alpha$

$$\mathbf{t}_\beta \approx \mathbf{t}_\beta^{adh}$$

$$\mathbf{t}_\alpha = -\nabla_s \cdot \varsigma_{\alpha\beta} + \left( \beta_\alpha \beta_\beta \int_{\partial\Omega_\alpha} \mathbf{n}_\alpha \otimes \mathbf{s}_{\beta\alpha} v(s) dS_\alpha \right) \cdot \mathbf{n}_\alpha, \ \forall \mathbf{x} \in \Gamma_{\alpha\beta}(\alpha) .$$

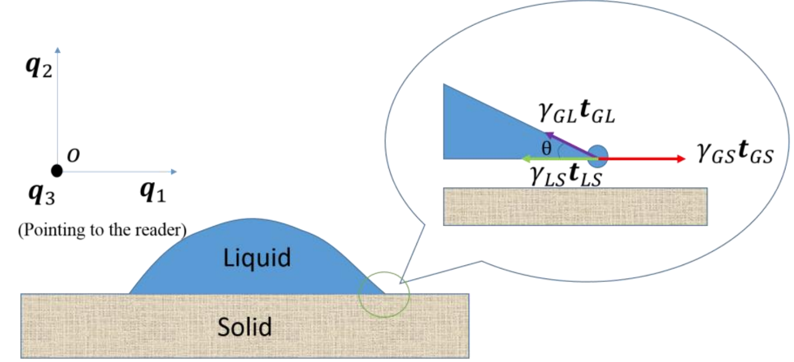
$\alpha \rightarrow \beta$

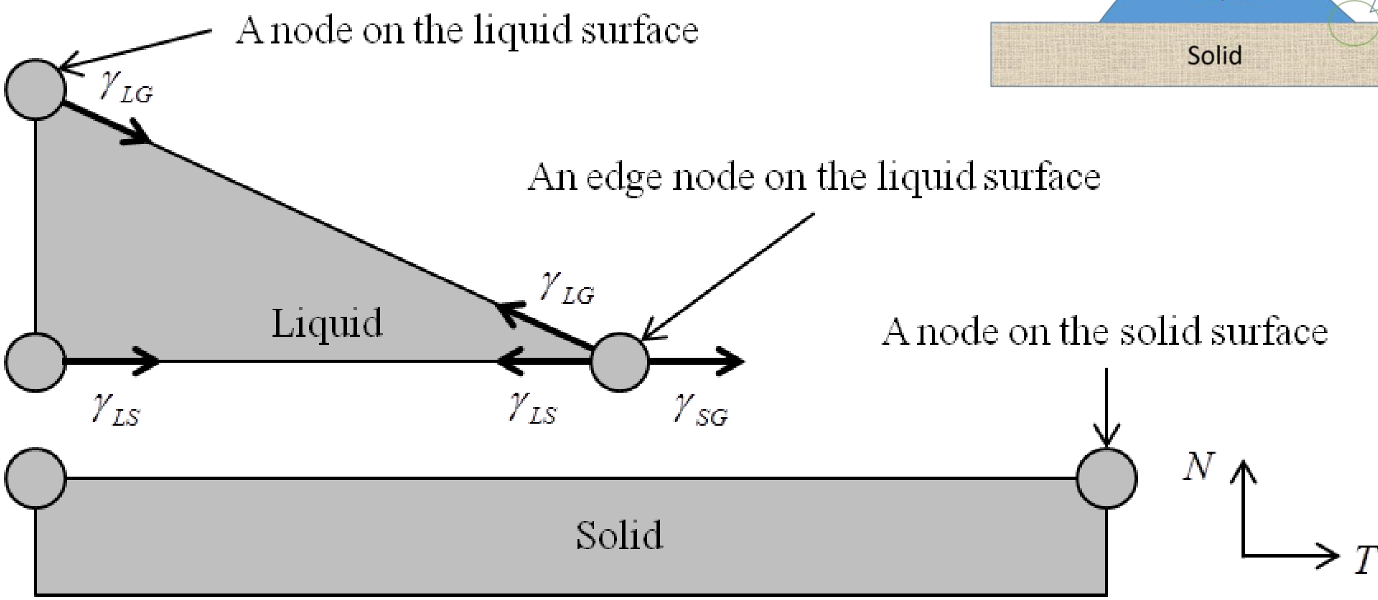
$$\mathbf{t}_\alpha \approx \mathbf{t}_\alpha^{adh} = \boldsymbol{\sigma}_\alpha^{adh} \cdot \mathbf{n}_\alpha = -\boldsymbol{\sigma}_\alpha^{adh} \cdot \mathbf{n}_\beta \qquad \boldsymbol{\sigma}_\alpha^{adh} = \left( \beta_\alpha \beta_\beta \int_{\partial\Omega_\beta} \mathbf{n}_\beta \otimes \mathbf{s}_{\alpha\beta} v(s) dS_\beta \right)$$

$$\mathbf{t}_\beta = -\nabla_s \cdot \varsigma_{\alpha\beta} + \left( \beta_\alpha \beta_\beta \int_{\partial\Omega_\beta} \mathbf{n}_\beta \otimes \mathbf{s}_{\alpha\beta} v(s) dS_\beta \right) \cdot \mathbf{n}_\beta, \ \forall \mathbf{x} \in \partial\Omega_\beta$$

**Li and Fan [2015], Proc. R. S.**

# A Simple Case

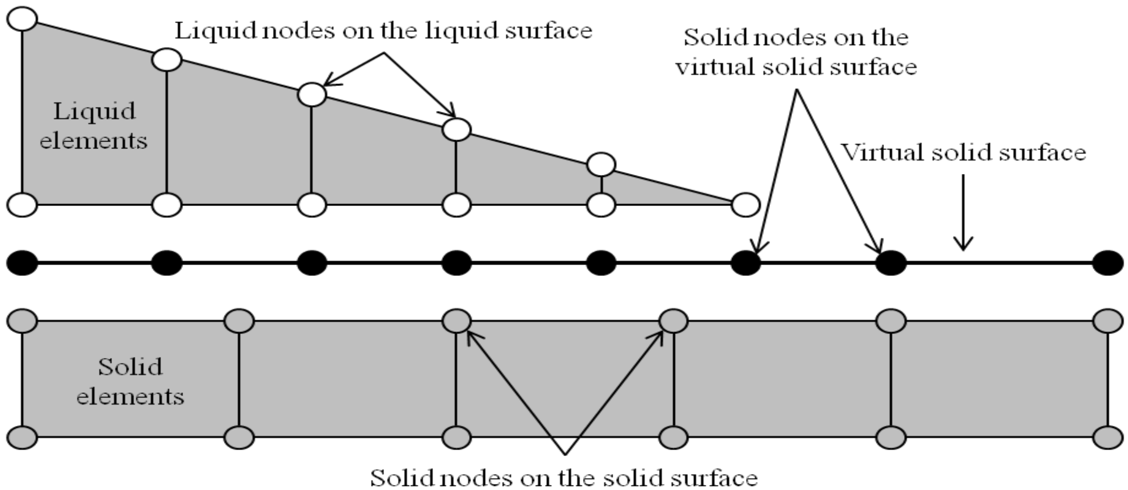


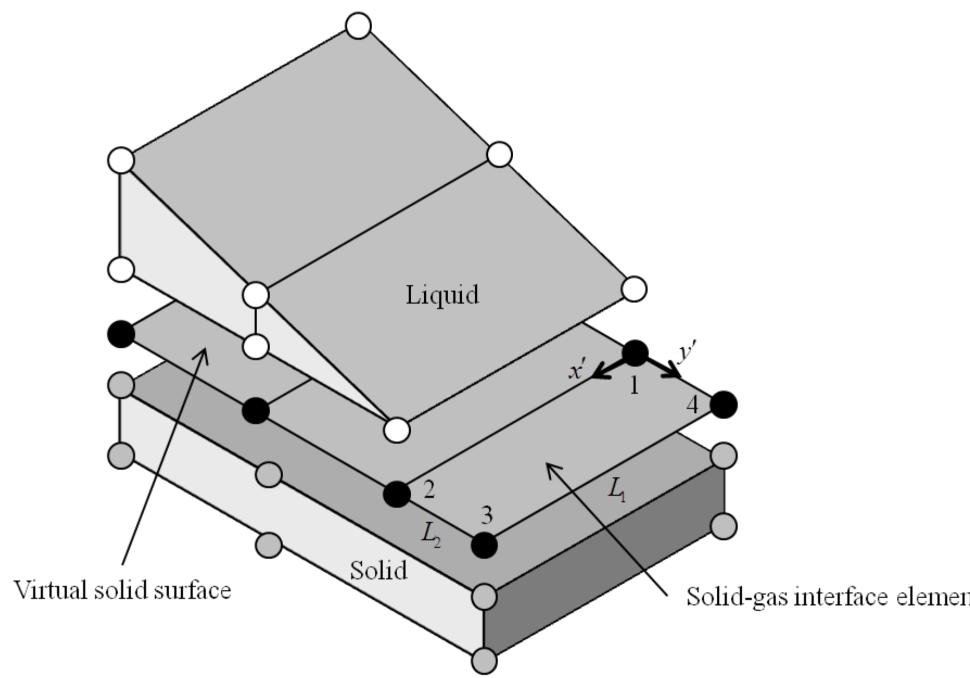




For the constant surface stress,

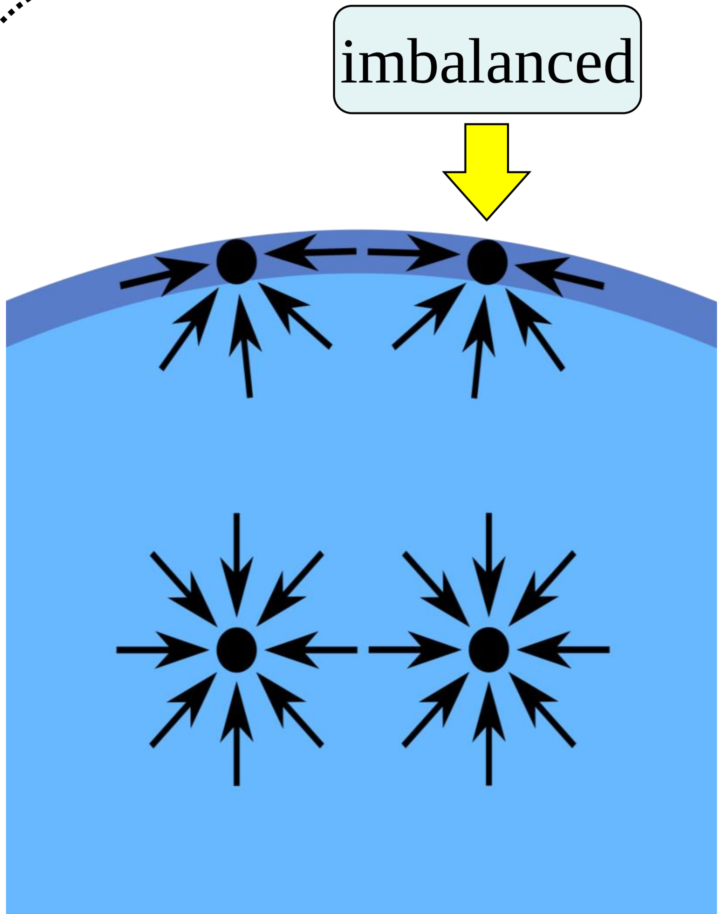
$$\varsigma^{LS} = \gamma_{LS}\mathbf{I}_s^{(LS)},\ \varsigma^{LG} = \gamma_{LG}\mathbf{I}_s^{(LG)},\ \text{and}\ \varsigma^{SG} = \gamma_{SG}\mathbf{I}_s^{(SG)}$$

where $\mathbf{I}_s^{(LS)}, \mathbf{I}_s^{(LG)}$, and $\gamma_{SG}\mathbf{I}_s^{(SG)}$ are the unit tensors on LS, LG, and SG interface.


Liquid nodes on the liquid surface
Solid nodes on the
virtual solid surface
Liquid
elements
Virtual solid surface
Solid
elements
Solid nodes on the solid surface


Liquid
x′
y′
1
4
2
3
L1
L2
Solid
Virtual solid surface
Solid-gas interface element

# Cell/Air boundary(surface tension)




The resulting traction,

$$\mathbf{t} = \sigma\mathbf{n} = -\gamma_0 \kappa \mathbf{n}, \ \forall \mathbf{x} \in \Gamma_{\text{cell/air}}$$

mean curvature,

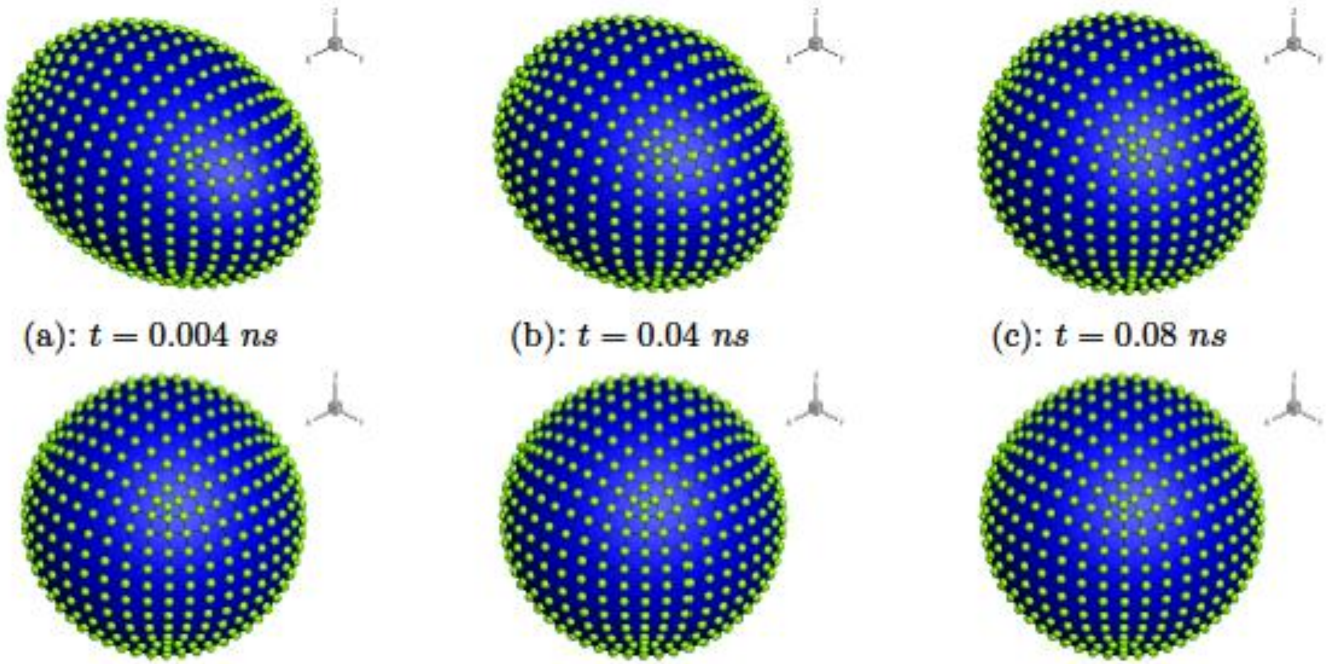
$$\kappa = \text{div}\left[\mathbf{n}\right]$$

unit out-normal,

$$\mathbf{n} = \alpha \mathbf{F}^{-T}\mathbf{N}; \alpha = \left(\mathbf{N} \cdot \mathbf{C}^{-1}\mathbf{N}\right)^{-\frac{1}{2}}$$

# Pure Surface Tension Action

*On Multiscale Moving Contact Line Theory*

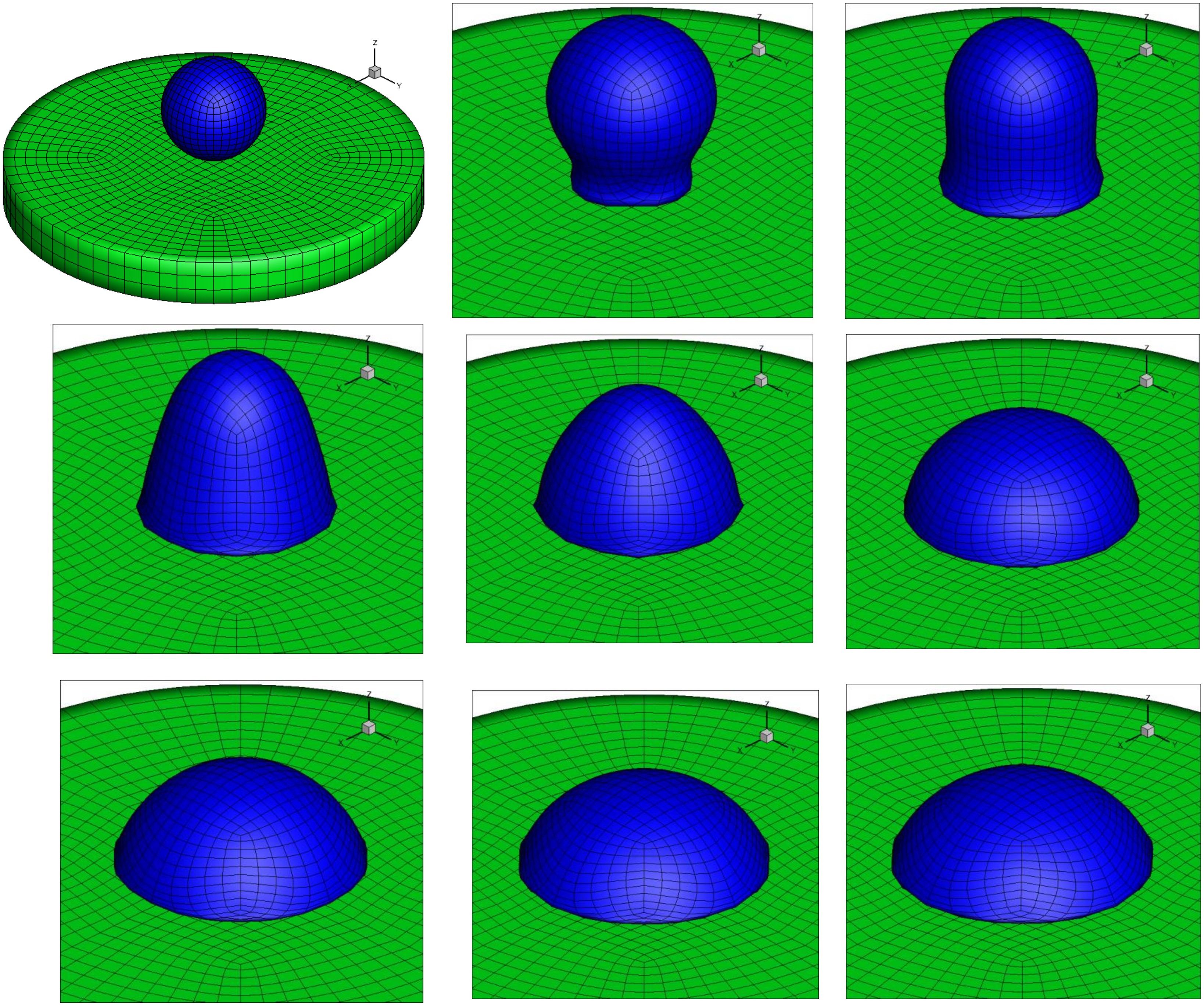


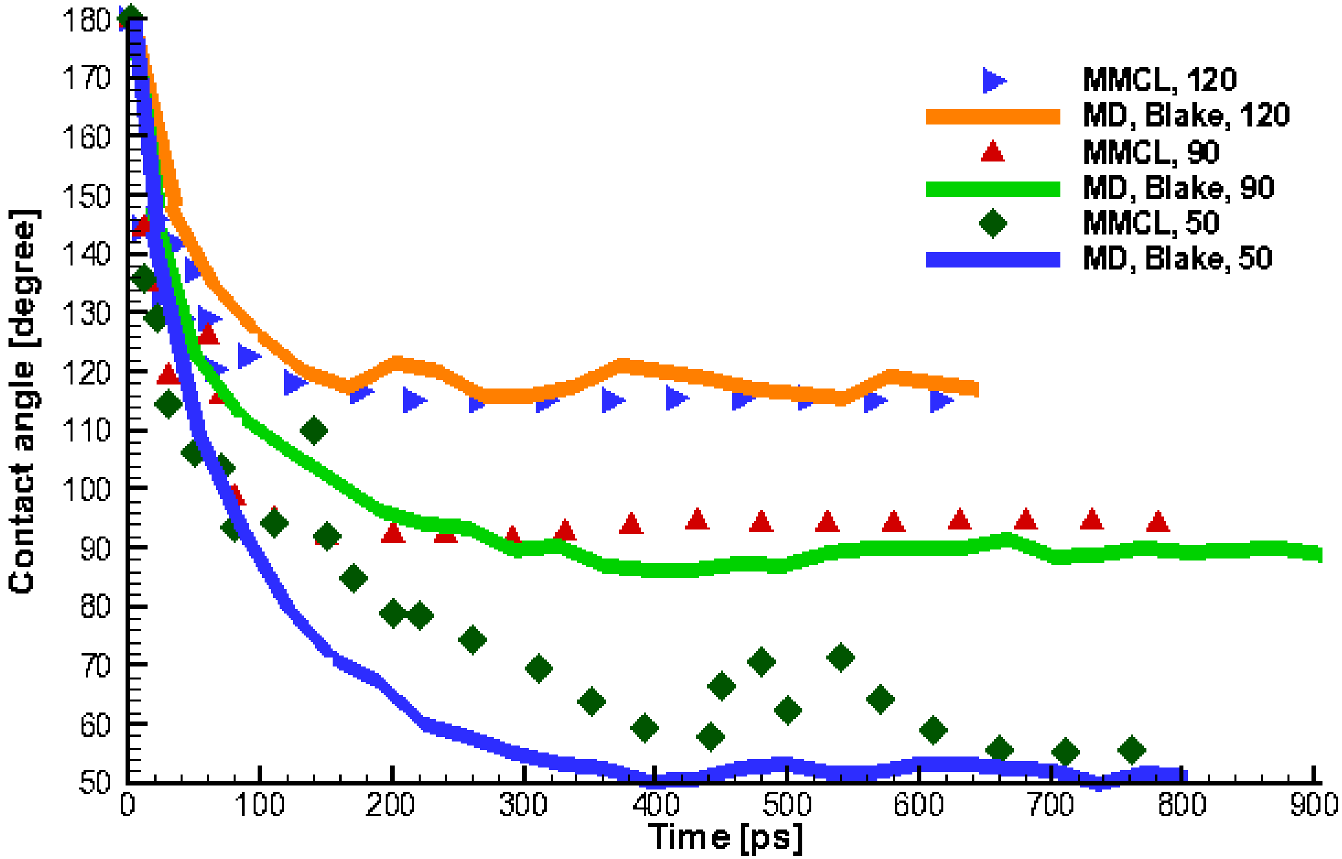
(a): $t = 0.004\ ns$ (b): $t = 0.04\ ns$ (c): $t = 0.08\ ns$

(d): $t = 0.2\ ns$ (e): $t = 0.28\ ns$ (f): $t = 0.4\ ns$

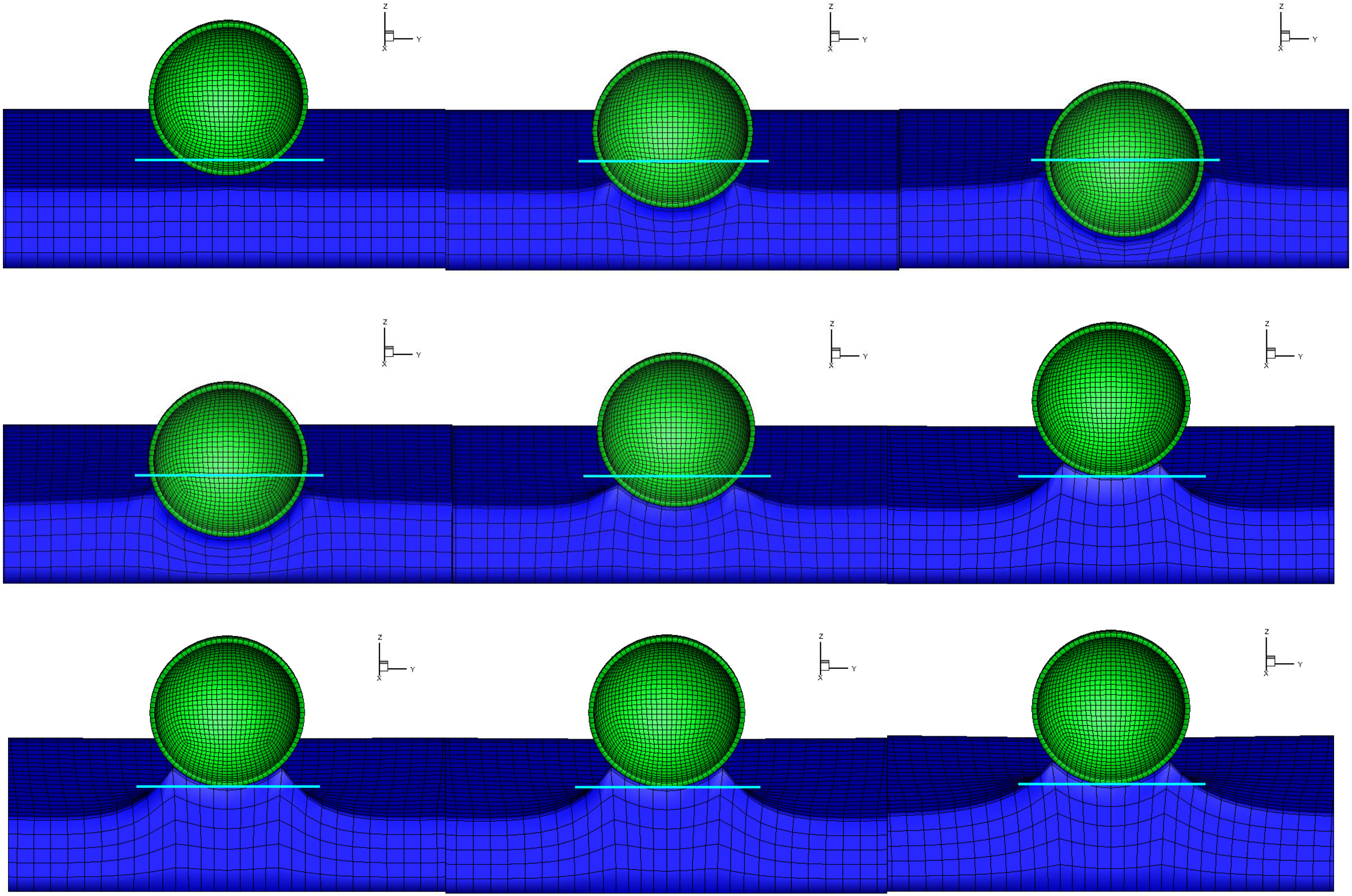
Time history of the simulation of a 3D ellipsoidal droplet embedded in atmosphere, driven by the surface tension effect.

**Li and Fan [2015], Proc. R. S.**






**Comparison of dynamic contact angles between MMCL and MD**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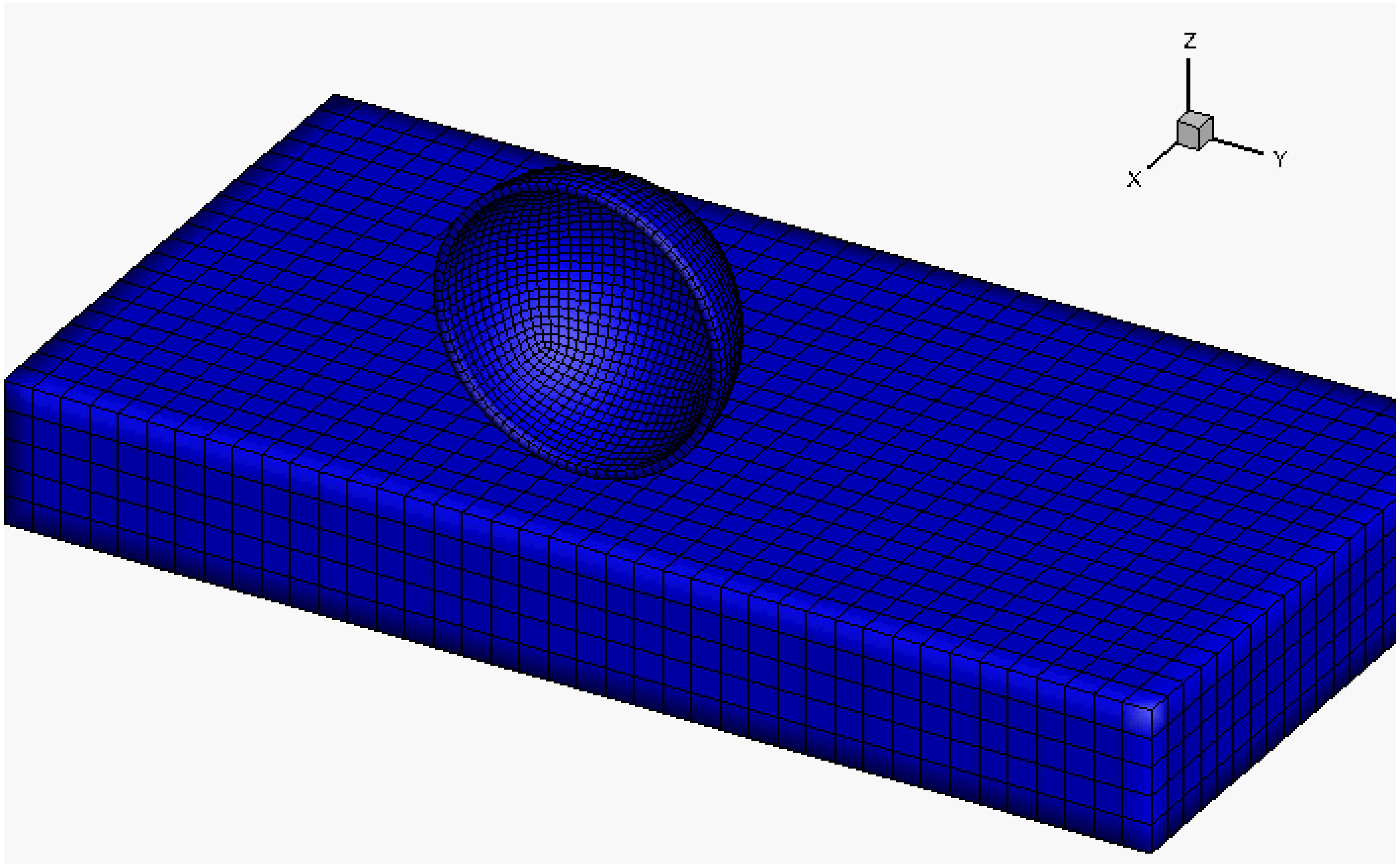
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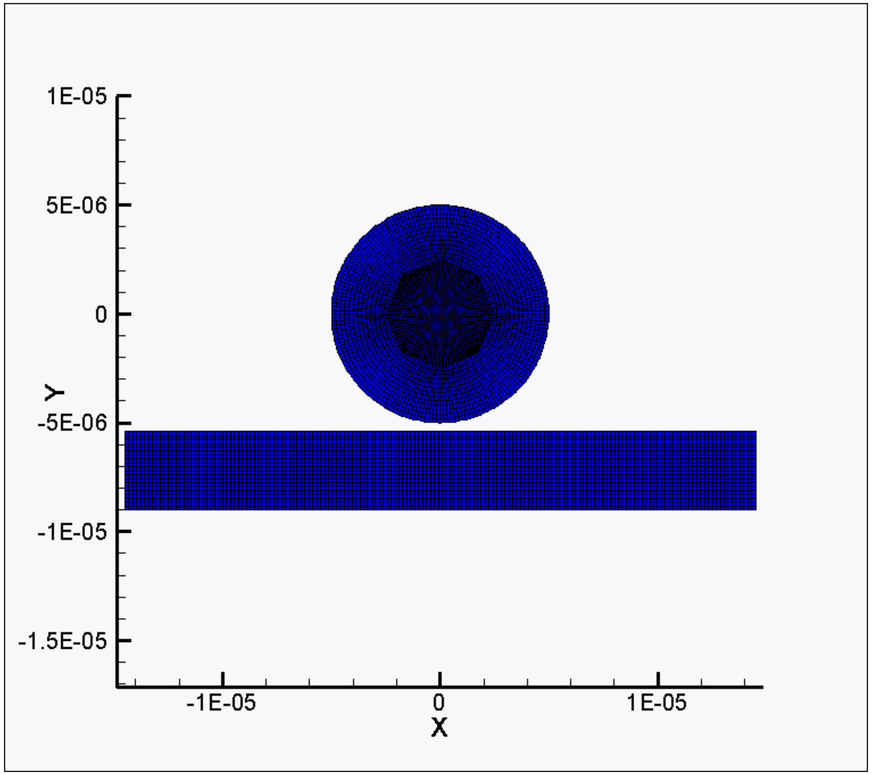
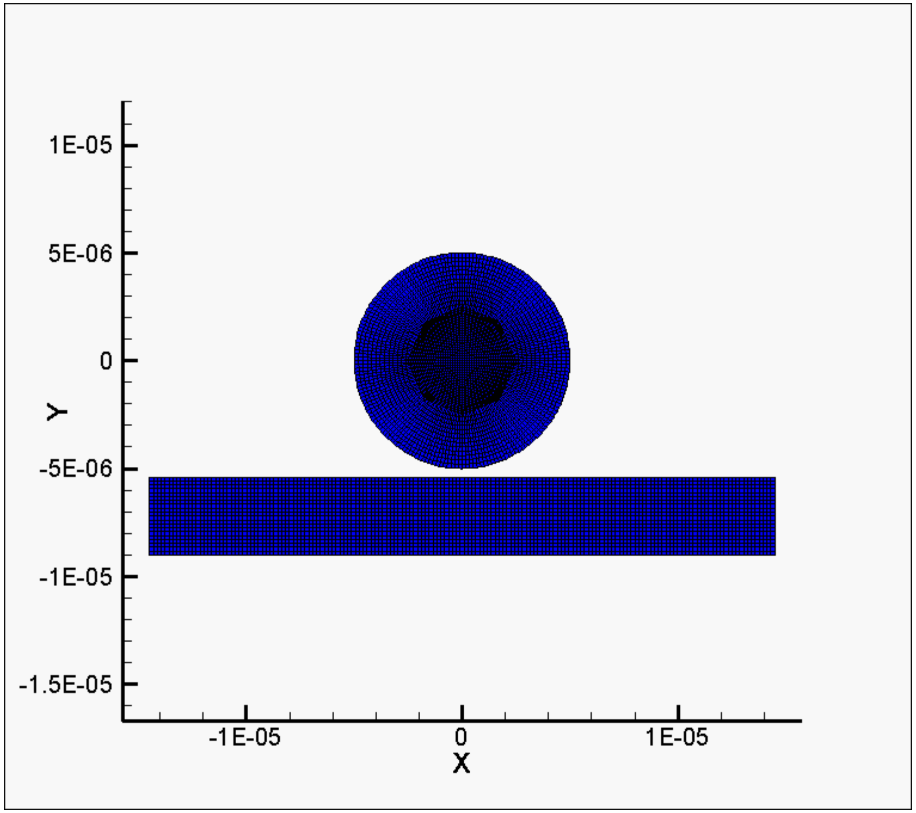
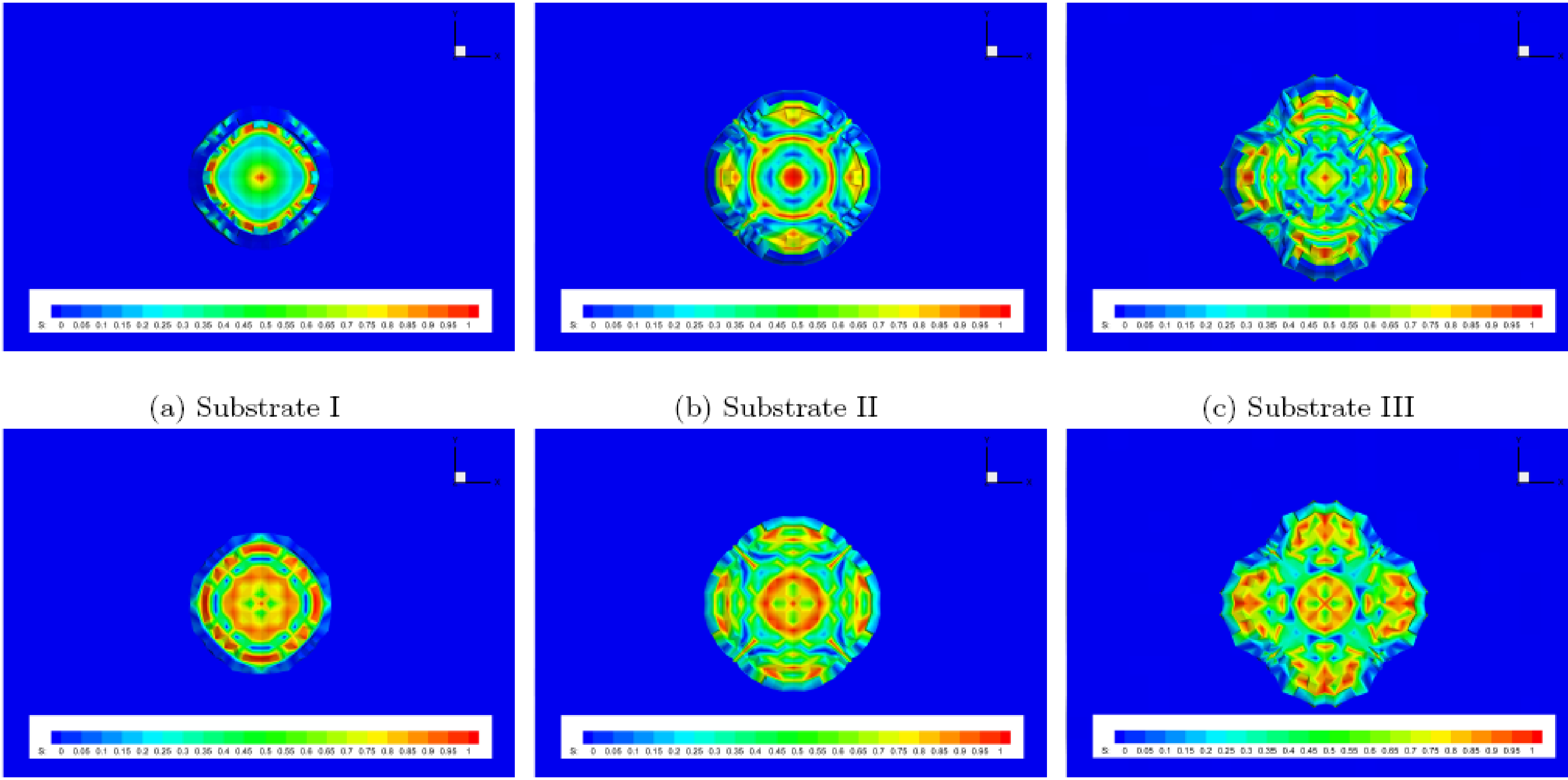



Stiffer Substrate

Softer Substrate





(a) Substrate I (b) Substrate II (c) Substrate III

(d) Substrate I (e) Substrate II (f) Substrate III

Orientation order parameter distribution during cell spreading on three different substraties

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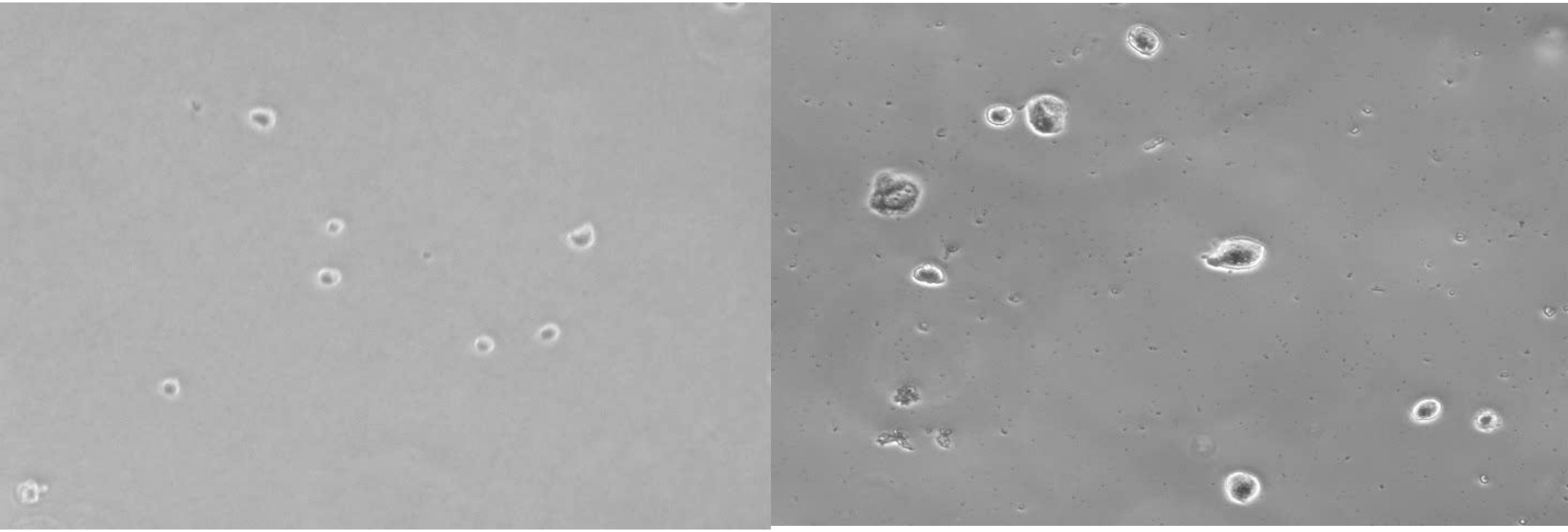
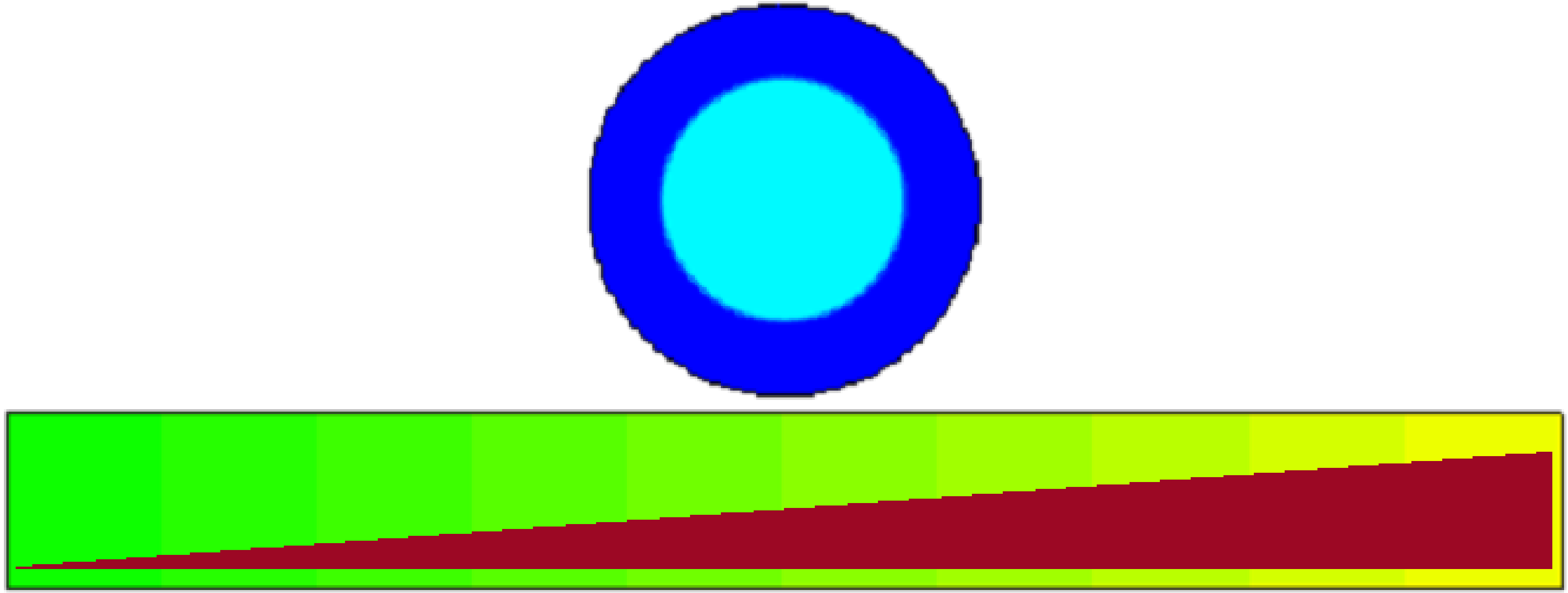
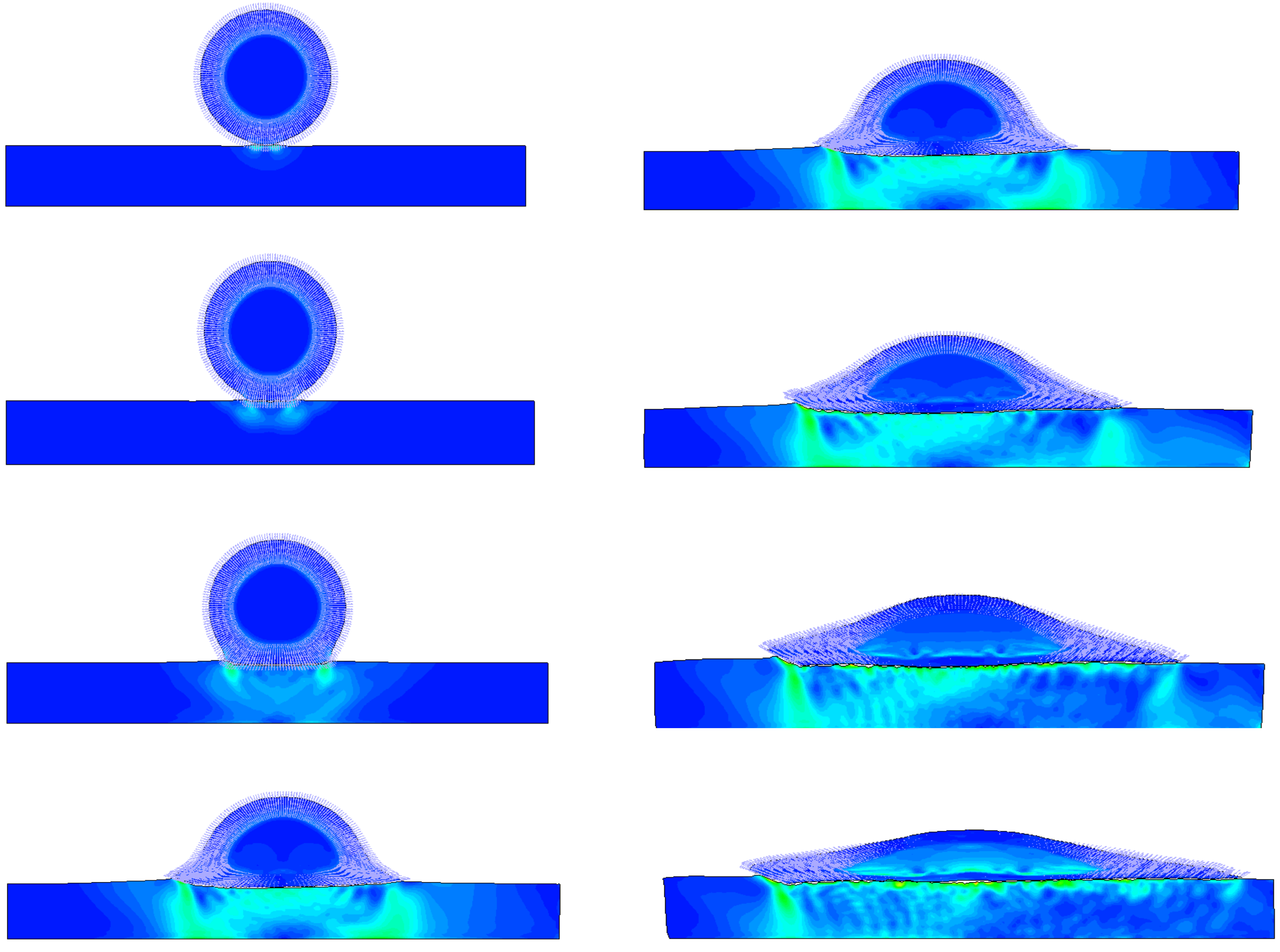


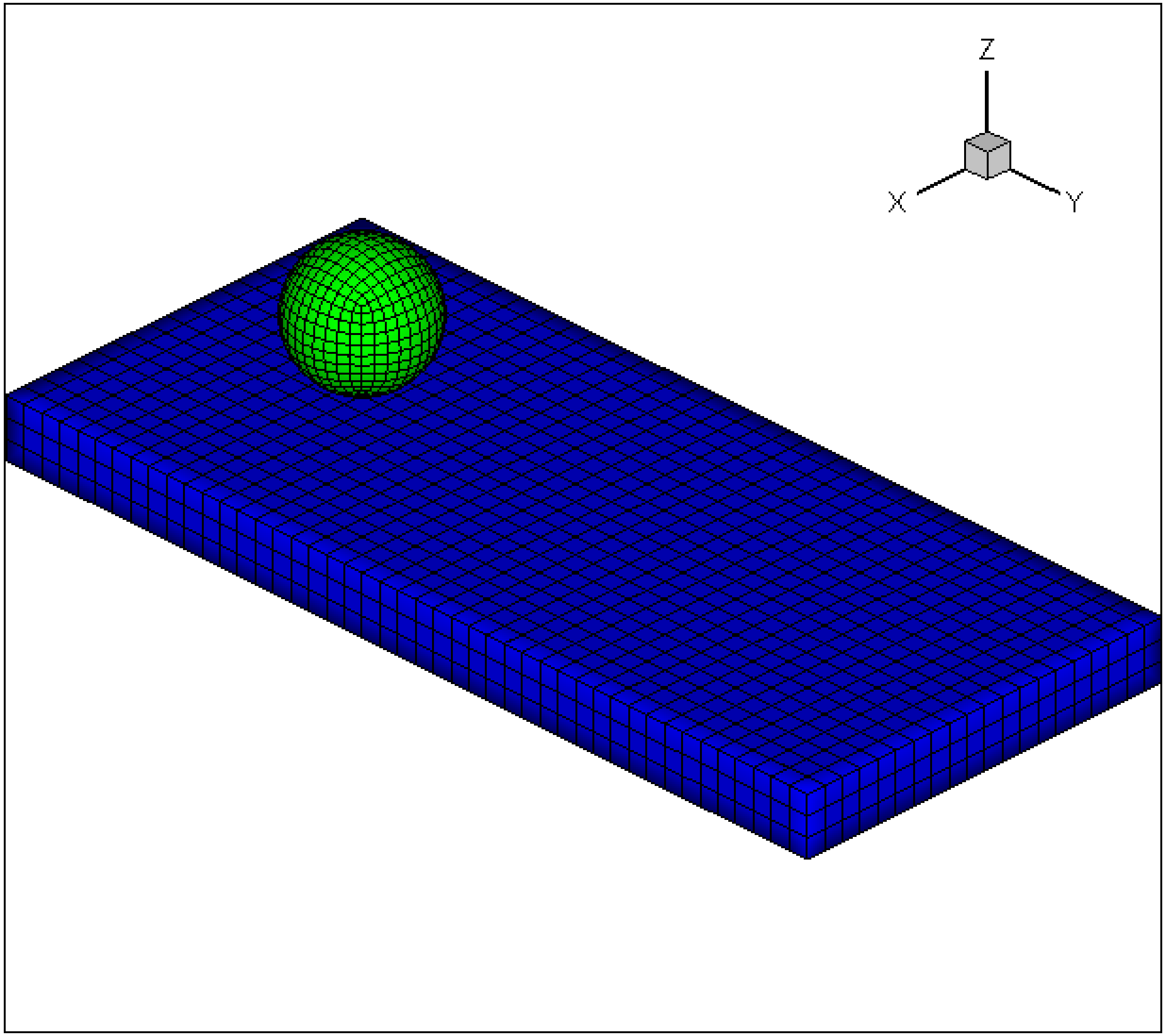
(a) 100 Pa gel substrate (b) Collagen coated glass (10 KPa)

(Ms. An-Chi Tsou and Dr. Song Li)



Direction of the Substrate Stiffness Increase





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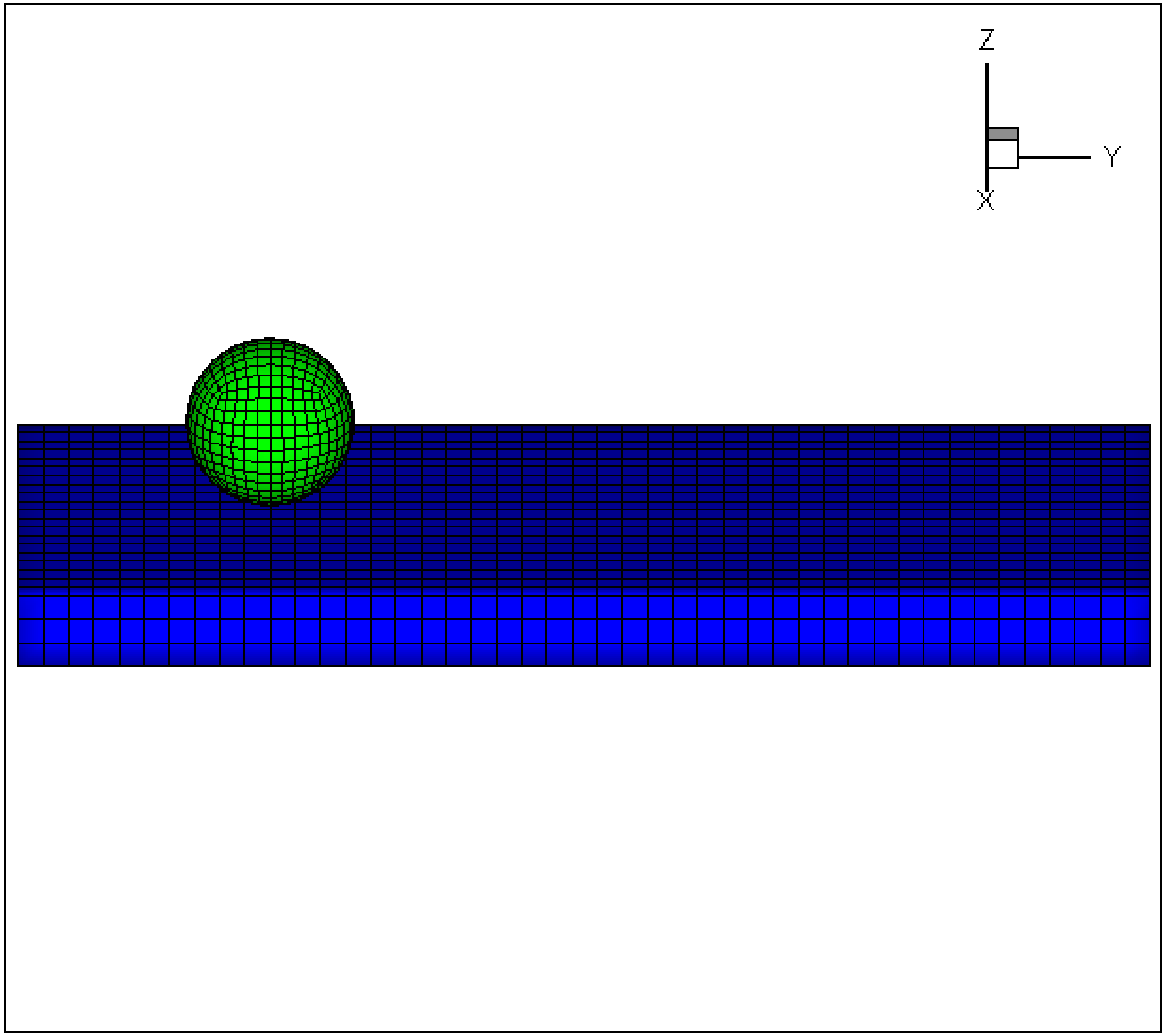

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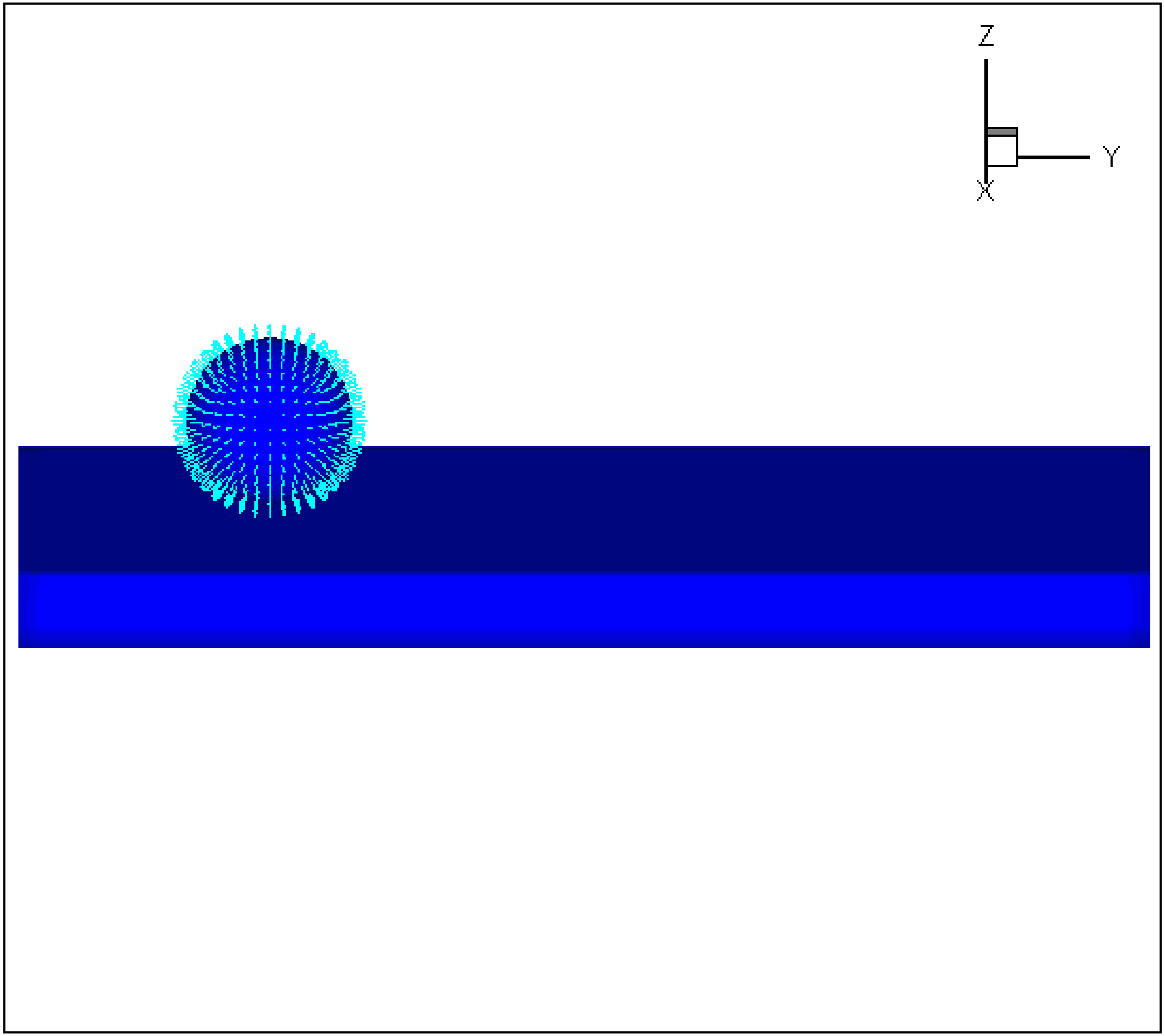

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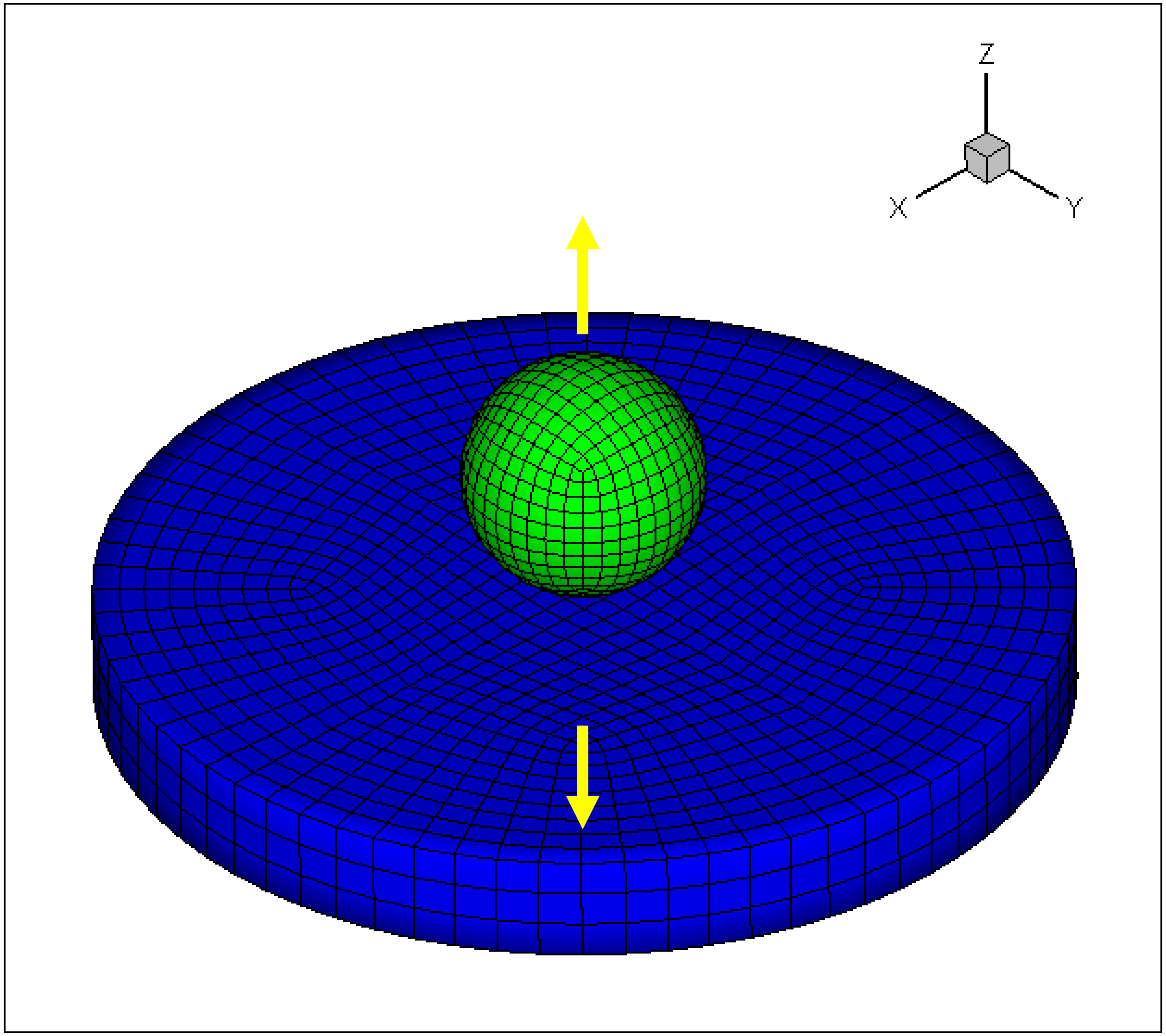

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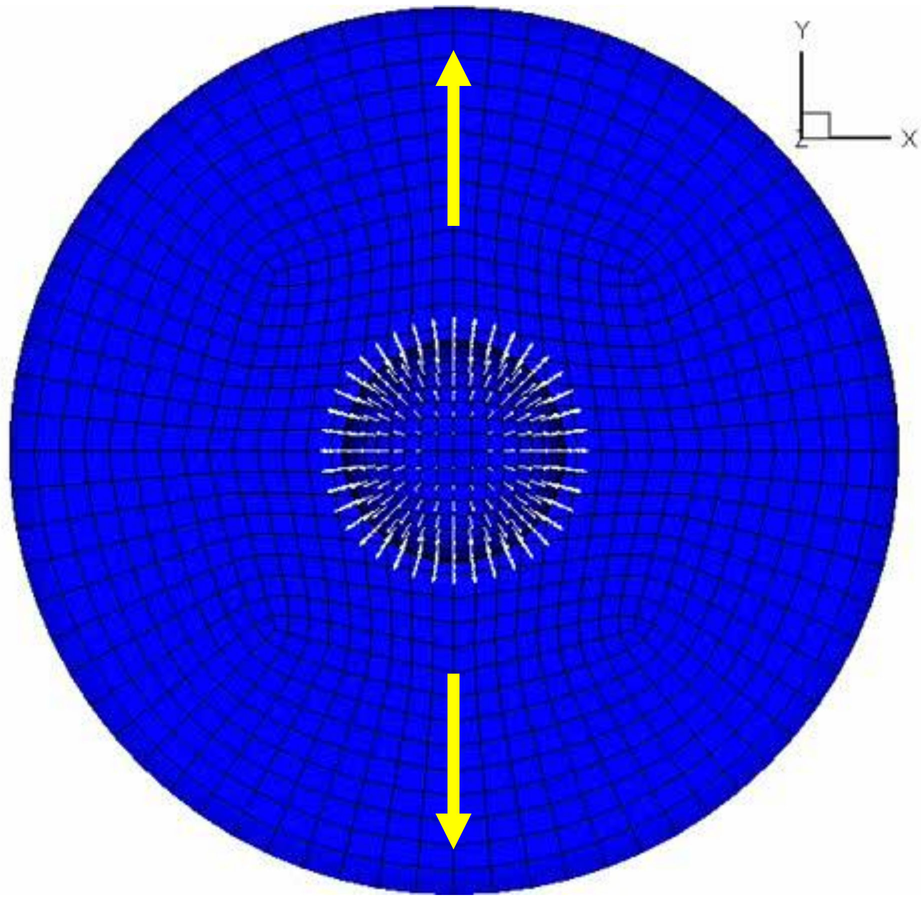
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